THE

VETERINARY JOURNAL

DECEMBER, 1909.

THE LATE MR. JAMES KING, M.R.C.V.S.

By the death of Mr. James King the Corporation of London has lost a valuable servant and the veterinary profession an ardent supporter of its rights. A native of Liberton, in Midlothian, Mr. King graduated from the Royal (Dick) College in Edinburgh in 1887, and at once went as assistant to Mr. Bazley, in Leominster, where he gained a good insight into the working of a large cattle and farming practice. After staying there for about two years, he commenced practice on his own account in Liberton, but when the appointment of Assistant Inspector of Markets to the Corporation of Edinburgh fell vacant, he applied and was at once selected.

This gave him the opportunity of following up the study of meat inspection and its branches, and three years later he was appointed Chief Inspector of Markets to the City of Manchester.

At the time of his appointment there was considerable feeling expressed amongst the traders and butchers that a veterinary surgeon should be selected for the position; but Mr. King's geniality and tact soon altered all this, and before he had been there very long his services were so much appreciated and the duties allotted to him increased to such an extent that two assistants were given to his department, and, by special request, these were duly qualified members of the veterinary profession. The City of Manchester was practically the pioneer of the cities of England in the attention paid to proper meat inspection, and this has been due in a very great measure to the efforts of Mr. King and the successful result of the experiment made in appointing him as the Veterinary Inspector.

Mr. King stayed in Manchester for six years, leaving with the good wishes of all his colleagues to occupy the position of Chief Veterinary Inspector to the Corporation of London. To this position has been added several other appointments, one of which gave him control of the Islington Market, and another the control of measures regarding glanders in the city area.

The students of the London College knew him well, for practical demonstrations were given regularly by him to Sir John McFadyean's classes; and to all he was ever courteous and eager to give ready help. Specimens were provided in plenty, and the practical demonstrations were always successes.

The Royal Sanitary Institute, too, secured his services as a lecturer and as an examiner, and on several public occasions he delivered lectures, notably last year at one of the conferences on tuberculosis.

His place will be hard to fill, and it is a matter of great regret for the profession that he should thus suddenly be cut down in the flower of manhood.

With the next volume of the Veterinary Journal, commencing January next, there will be introduced several changes. In the first place, it is with great regret that we announce the retirement of Professor Williams from the Editorial staff, a step which he has found necessary owing to the great pressure of other work. However, he has kindly promised to support us still, and to contribute to our pages from time to time. We are endeavouring to fill his place by another eminent veterinarian, who has practically consented to act, but as final arrangements have not yet been possible owing to the distance he is away and the length of time it takes for letters to pass between us, it would be premature to name him.

It is also our intention to increase the size of the Veterinary Journal, and, by request, to print it in a little bolder type. Other changes may be introduced from time to time. The subscription, however, will remain the same as at present.

Some of the most interesting features in the Journal have been the records of clinical cases, and we earnestly ask our readers to assist us in this direction better than they have done hitherto. We realize fully that many practitioners may find it difficult sometimes to spare enough time to write accounts of their interesting cases, but they would, we feel sure, be fully repaid by knowing that they had contributed even a little to the sum total of our knowledge. Failures as well as successes should be recorded, as both are equally instructive. We thank our present and past contributors, and trust other readers will assist us in this direction better than they have previously done.

Editorials.

THE STUDY OF CANCER.

We doubt if there was ever any period in the history of the world when so much good work was being carried out to find the causes or undermine the effects of those great scourges of the whole animal kingdom as at the present time. Yet in spite of an army of workers progress is certainly slow, and perhaps more so in the field of cancer research than in any other. Numerous investigators throughout the civilized world are devoting their lives to the attempt to solve the mystery of causation of cancer, and although they are elucidating various aspects of the cancer question, the main point still escapes them. Progress is being made, certainly, and perhaps one of the most important lines of progress is the explosion of numerous misconceptions of cancer, the exclusion of which enormously cuts down the field of investigation and enhances the prospect of ultimate solution of the question by permitting greater concentration of energy in research. Probably the finest published contribution to the study of cancer up to the present is the paper by Dr. Bashford presented to the International Veterinary Congress at The Hague, a portion of which we reproduce elsewhere in this issue of the Veterinary Journal. Unfortunately, the whole paper is too long for us to reproduce in its entirety, but we have endeavoured to retain the most important parts of it.

Some of the results of the work, in which Dr. Bashford was assisted apparently by Drs. Murray and Cramer, are of a negative character, while others are of a positive character. With the former we include the conclusion arrived at concerning the probability of an intracellular virus being the cause of cancer, and concerning the theory of retained or re-acquired embryonic characters of certain cells. In view of their work, and for reasons adduced by Bashford, he regards those theories as no longer tenable and characterizes them as unnecessary mental luxuries. Another, but tentative negative conclusion of the very highest importance concerns the question of heredity. Bashford and his collaborators made very extensive investigations on this point with mice, which are specially suited to such observations on account of their

short life enabling many successive generations to be observed. It is also possible to note with precision the condition of many generations of ancestors. In a few years they will be able to produce numerous figures to decide this question, but up to the present there is no indication that the popular idea will be supported. Indeed, the evidence decidedly points the other way, as the proportion of cases of cancer developing in mice of cancerous parentage only corresponds with the general proportion of cases in all mice. In fact, the development of cancer in such cases appears to conform only to the general rule of "age incidence." Although not wishing to anticipate the results of their observations, which are still continuing, Bashford says, "We have not as yet obtained any indication that cancer is inherited. It appears to be very doubtful whether there is transmitted even so much as either a constitutional or a local predisposition." If this should turn out to be correct it will bring comfort to thousands who live in fear because one of their parents died from this awful disease.

Of their positive conclusions we may note those referring to the age incidence of the disease, and to possible immunization. The statistics as to the increased frequency of malignant new growths in the human subject with advancing age are clearly supported and confirmed by their observations on mice of their own breeding. Obviously, advancing age *is* an important factor in the occurrence of the disease.

One of the most interesting features of Dr. Bashford's paper is the portion referring to the possibility of producing immunity against cancer. He and his collaborators, as also Ehrlich and others, have shown that any particular tumour of a species (*e.g.*, a carcinoma of a mouse) may induce protection against itself and other tumours of its kind by "vaccination." But as "vaccination" in this instance is meant to indicate the transplantation of tumour material without producing a growing tumour, the process is decidedly dangerous. Moreover, any attempt by physical or chemical agency to attenuate the tumour or to rob it of its power of growth on transplantation, not only robs it of its power of growth, but may be followed by hypersensitiveness, and so may increase the susceptibility to the particular variety of tumour being used. Bashford states that protection is only produced

against the particular type of cancer used. Ehrlich believes in "pan-immunity," or that immunity set up by one variety will also protect against other varieties of malignant new growths, that carcimona vaccination will protect against other carcinomata and also against sarcomata. Both Bashford and Ehrlich apparently agree that a very remarkable phenomenon may occur in propagating carcinomata—namely, that they may become replaced by sarcomata. If that be the case, then there must be some more intimate connection between these malignant tumours than is believed at present, and it would certainly add weight to Ehrlich's hypothesis of "pan-immunity."

But a more interesting claim still is made by Bashford on this question of protection. He asserts that protection against malignant growths may be produced by "vaccinating" them with *normal* tissues of their own species. He says: "Normal tissue may protect absolutely against the transplantation of an homologous tumour—*e.g.*, mamma against mammary carcinoma, or skin against squamous-celled carcinoma."

It will thus be seen from the foregoing what enormous strides are being made, and in view of them the all-important matter of the actual exciting cause of cancer may be discovered almost any day. That it may be soon is our earnest hope.

SPECIFIC CHRONIC ENTERITIS OF CATTLE—JOHNE'S DISEASE.

As we indicated in our summary of the proceedings of the International Veterinary Congress at The Hague, the above subject was one of those which occupied an important part of the discussions. We stated on that occasion that there is some divergence of opinion as to whether or not the bacillus of this disease is a variation of the tubercle bacillus of Koch. Some think it is the bacillus of avian tuberculosis; some that it is the bovine bacillus becoming saprophytic. We are unable to accept either of the two latter views, and we are supported in this respect by Bang, McFadyean, Frothingham, and others.

One very strong argument against those views is the fact that in Jersey tuberculosis of cattle is unknown, though Jersey cattle are

very susceptible to infection, and yet this specific chronic enteritis is very common in the island. At the Congress it was not possible to come to any unanimous decision on that point, but a very important practical point was agreed upon—viz., that similar steps should be taken against it as against cows affected with open tuberculosis; they should be slaughtered, for undoubtedly the chief means of spread is the dung of affected animals.

The whole question of this disease is of great importance, so we publish for the advantage of our readers a short summary of the papers presented to the Congress on this subject. It must be remembered, too, that the writers of those papers are all eminent men whose opinions are worthy of the greatest consideration.

With regard to the diagnosis of the disease, a very important statement was made by Professor Bang to the effect that his son had found that affected cows, though free from ordinary tuberculosis, would give a reaction to tuberculin prepared from avian tubercle bacilli. This matter, of course, requires further investigation for confirmation or otherwise, and if it should be well founded we should consider it one of the most important advances in cattle pathology, and would save thousands of pounds to agriculturists since it would be possible to detect the disease in the earlier stages while it was yet possible for the affected animals to be fattened even if not cured.

General Articles.

ON MELANOSIS OF THE LUNGS AND LIVER, AND MELANIN FORMATION.

BY PROFESSOR A. E. METTAM, B.SC., M.R.C.V.S., M.R.I.A., PRINCIPAL OF THE ROYAL VETERINARY COLLEGE OF IRELAND.

THE pigmentation of the skin and its appendages is due to the presence of a pigment known as melanin. This pigment is contained in the cells of the rete Malpighi of the epidermis and those epithelial cells which build up the hair and horn. It was considered, and still is considered by some, that this pigment is derived from the blood, that the colouring matter is a derivative of hæmatin ; but there are reasons for believing that the origin is altogether different. I propose in this note to give some views as to the origin of melanin, and incidentally to describe its occurrence in unusual sites.

Quite recently I obtained through the instrumentality of Mr. Watson, Veterinary Inspector of the Dublin Corporation, the liver and lungs of an ox that had been slaughtered for food. The animal was of a red colour, in good condition, and, as far as I can ascertain, showed nothing abnormal, save for the organs mentioned. The lungs were free from any pathological lesion, except for a couple of fluke cysts and the abnormal colouration. Patches, varying in size from the palm of the hand to that of a single lobule of lung, were intensely black, ink-black, and they were rendered all the more striking in appearance by the normal pinkish red of the surrounding unaffected lung structure. The largest areas were in the anterior lobe of the right lung and the caudal lobe of the left lung towards the free border of the lung in both instances, and on cutting into the pigmented areas the colour was found to extend through the lung parenchyma from pleura to pleura. In the smaller patches the colour involved only a single lobule, or it maybe two, but it was confined to the lobule or lobules and did not extend into the deeper parts of the lung. In a few lobules, where the condition was evidently not so far advanced, the colour was rather greyish than black, and in an odd lobule or two all the stages, from the normal pinkish red to dark grey, could easily be seen. I had only the opportunity of examining a portion of one bronchial gland—the others had been removed before I got the specimen—but the gland was pigmented in isolated areas in the cortical portion of the gland. It is not uncommon for the bronchial glands to be pigmented without undue or markedly abnormal coloration of the lungs, but the gland mentioned had an excess of pigment and it was not evenly distributed.

The liver was not increased in size. It was cirrhotic, due to fluke invasion at some prior date, and there were a number of angiomata of small size scattered through the liver. In parenthesis I may mention that cirrhosis of the liver and angiomata occur commonly together. Of course, cirrhosis without angiomata is far from rare, but in my experience never the latter without some degree of the former. I hope at some future time to return again to this lesion. Beneath the serous covering could be seen extensive areas of pigment, quite black and these areas were scattered over the whole surface of the

liver. They varied in size from 3 in. square downwards. Incising the organ through the pigmented area the colour, was found to be in the capsule and ramifying in fine, delicate arborescent lines into the liver-substance, or, rather, between the lobules. Thicker lines indicated the presence of a vessel embedded in Glisson's capsule. The pigment did not extend deeply into the liver from the capsule, not more than an inch. On cutting into the liver and following up the portal systems, Glisson's capsule was observed to be of a greyish colour, and apparently the pigmentation was following the connective tissue in its ramifications.

Pieces of the lung, bronchial lymphatic gland and liver were fixed, and after dehydration were passed through xylol into paraffin, em-

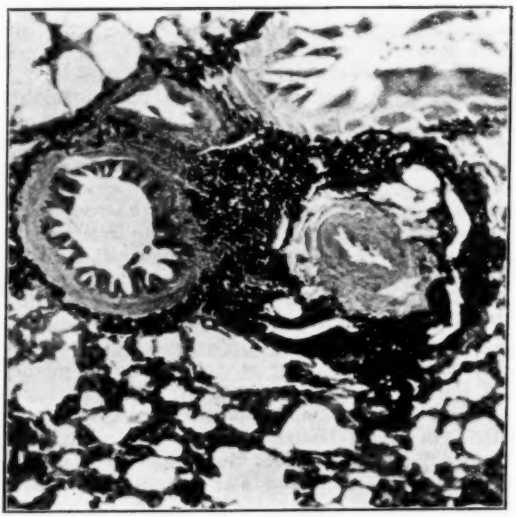

FIG. 1.—Section of lung showing melanin in the perivascular tissues of pulmonary artery. Some pigment is seen in the corium of mucous membrane of the bronchus.

bedded and cut. Sections were examined unstained, stained by hæmatoxylin and eosin, hæmatoxylin and van Gieson's stain (modified), eosin and toluidin blue, methyl blue and eosin, &c., clarified in the usual way after dehydration and mounted in balsam. The modification I use of van Gieson's stain I find particularly valuable, as the colour of the hæmatoxylin may be retained, or largely so, if the sections are not kept too long in the van Gieson mixture. I dilute down the the stain as made up for connective tissue staining, according to the usual formula, by adding three parts of half-saturated picric-acid solution in water and five parts of water, until the solution resembles a dilute picro-carmine tint. After the section has been stained with hæmatoxylin, and differentiated in the usual way and washed in water, the slide upon which the sections are fixed is flooded with the van

Gieson modified mixture. This is immediately poured off and the slide again flooded with the stain. This is run off, and without washing in water the sections are dehydrated, clarified, and mounted in balsam. The nuclei are bluish, protoplasm yellow, red corpuscles yellow, connective tissues, even the most delicate fibrils, ruby-red. The results, when successful, are extremely satisfactory and convincing.

The Lung.—The pigment is scattered through the whole of the parenchyma of the part involved. The thin alveolar walls carry masses more or less large and more or less irregular in shape. In this section the pigment is found to be in the form of minute granules considerably less than 1 μ in diameter. They look like minute brown

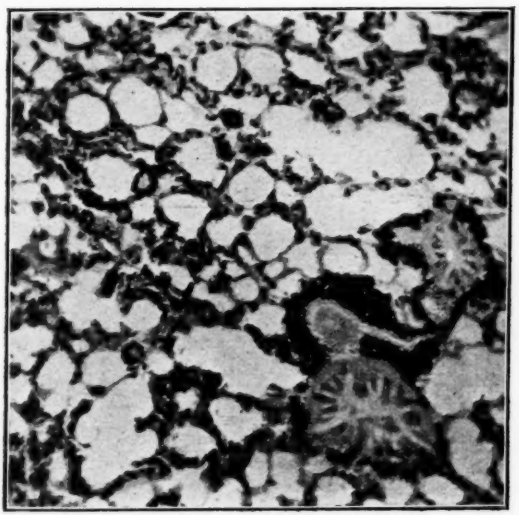

FIG. 2.—Section of lung. The pigment is seen in the walls of the alveoli, around bronchi and an artery.

cocci. Aggregations of these minute spherules give rise to lumps of pigment which obscure the nuclei of the cells carrying it. It is difficult to decide if the cells are in the walls or on the walls of the alveoli, but I have satisfied myself that in most instances they are in the tissues of the alveolar wall. The walls are in some parts atrophied and thin, and have ruptured owing to over-distension (emphysema); in other parts of the same sections the walls are thickened from interstitial changes, and there is evidence of collapse. The greatest accumulations of pigment are to be found in connection with the perivascular lymphatics. The pulmonary vessels are thickly ensheathed with large masses of pigment apparently contained in large branching cells. Similar accumulations may also be found in the lymphatic tissue of the interlobular connective tissue, apparently

bordering lymphatic vessels and clefts. The chromatophores, or pigment-bearing cells, may also be found in the connective tissues of the bronchial wall, both internal and external to the muscular layer. Those internal to the bronchial muscle pass quite close to the epithelium of the bronchus, and even pass between the bronchial epithelial cells. In the bronchi amidst the cellular *débris* there is some small quantity of blood which probably escaped at death. Cells containing melanin may be seen. This melanin has in part been coughed up from the alveoli and in part reached the lumen of the bronchus through the mucous membrane of the part.

The pleura proper was not pigmented, but around the vessels in the membrane, and especially where the interlobular connective tissue was attached, accumulations of chromatophores were found.

FIG. 3.—Section of liver. The pigment is seen in the connective tissue surrounding an isolated lobule. The liver is cirrhotic.

In sections of the pulmonary vessels, and also in some of the bronchi, hyperplasia of the walls was observed. The thickening in the vessels was chiefly the middle coat and adventitia; there was no proliferation of the internal coat, though the thickened arterial wall had almost obliterated the lumen. In certain of the bronchi the bronchial muscle had also hypertrophied.

Bronchial Gland.—Melanin was found in the gland, but not universally distributed through the sections. It was found in both cortex and medulla. Some of the pigment is extra-cellular, some of the granules have been phagocyted, but in other parts it is difficult not to believe that the pigment is in the endothelial cells of the lymph channels and in the cells of the delicate reticular tissue. The greatest

amount of the melanin is in the cortex, but there are many nodules in the cortex wholly free of pigment. Numerous eosinophilous cells were met with in the lymphatic gland.

The Liver.—The capsule is slightly thickened and in it are large chromatophores with numerous processes filled with pigment granules. These cells are in the lymphatic clefts and spaces. The pigment cells also pass into the connective tissue between the lobules, and are found in the connective tissue of Glisson's capsule of the portal systems. There is a moderate amount of cirrhosis in the sections examined, and in the newly formed connective tissue the pigment-bearing cells are found. A very interesting feature observed is the presence of pigment within the endothelial cells of branches of the portal vein, and the presence of melanin granules and even lumps

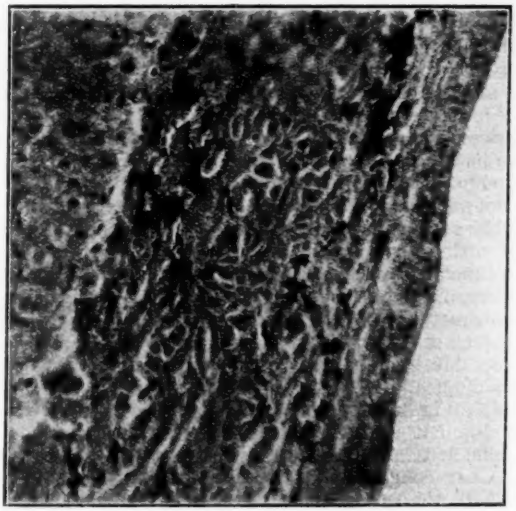

FIG. 4.—Section of liver shows thickened capsule containing large pigment-bearing cells.

of the pigment within the interior of leucocytes in the veins. The melanin is practically, however, confined to the connective tissue, but in a few places I observed pigment in Kuffner's cells of the sinusoids of the liver lobule. The hepatic artery and the bile-duct apparently are unaffected directly, though the connective tissue in which these are embedded, as mentioned above, contain the pigment-bearing cells.

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The substance we call melanin, the substance which is found in the skin, hair, horn, hoof, iris, choroid, &c., is of a dark-brown colour and intracellular or extracellular, and is in the form of minute granules or amorphous masses. Its colour is dark brown, not black, and its composition appears to vary considerably. It is remarkably

free from iron, though perhaps not absolutely so in every case, and it is remarkably rich in sulphur, some specimens containing as much as 10 per cent. Its poorness in, or the complete absence of, iron shows it not to be of blood origin, and the presence of sulphur points to its protein derivation. It is quite insoluble in all ordinary reagents except alkalies, in which some melanins dissolve readily, others with difficulty. Boiling hydrochloric acid even when strong scarcely affects it, but it can be bleached by oxidizing agents, as chlorine gas or chlorine water, or sunlight. It can be decomposed, yielding skatol, indol and melanic acid.

If melanin be injected into animals subcutaneously, it apparently is converted into a colourless substance, melanogen, which is excreted with the urine, and the urine, previously not abnormally coloured, now turns brown or blackish brown on standing. It is probably in this form of melanogen that the melanin is normally got rid of from the body, and it is probable that conditions which prevent the conversion of melanin into melanogen will conduce to pigmentation of the body. It may also be that the abnormal pigmentation observed in certain conditions may be due to an excess in the formation of melanin, and not wholly to failure in the conversion of the coloured melanin into the colourless melanogen. It is interesting to note that recently melanogen has been isolated from white hair, wool, and skin.

The amount of melanin present in the the body of the domestic animals has not been estimated, so far as I know, but Abel and Davis calculated that the amount present in a negro's skin was about 1 grm. In a case of melanosarcoma in man the liver was found to contain 300 grm. of melanin, and it was estimated that the subject contained at least 500 grm. in his body. That more than this is contained in the lesions sometimes observed in the horse I am convinced, as I have seen the spleen of a horse weighing 32 lb., and the enormous increase in bulk was due to a number of melanotic tumours varying in size from a child's head downwards. And also in the liver. This organ may contain an infinite number of melanotic new growths containing so much pigment that their structure can only be made out with extreme difficulty.

For a clear conception of the formation of melanin we have to look elsewhere than the tissues, normal or pathological, of man and the lower animals, though recent researches have demonstrated that the interactions resulting in melanin are essentially the same in all. In the sepia sac of the cuttlefish, the ink sac which the mollusc is capable of emptying to hide its retreat, an oxidizing enzyme has been found which has the property of producing black pigment by its action on tyrosin or other aromatic protein compounds. It is by a similar process that certain plants of Japan produce the black lacquer. When the plant is injured the escaping juice turns black owing to the action of an enzyme known as tyrosinase. This tyrosinase is also found in certain fungi. The melanin of the animal body is believed to be formed by the action of an enzyme or enzymes. V. Fürth urges strongly the view that melanin, both normal and pathological, depends upon the action of tyrosinase or allied enzymes in conjunction with autolytic enzymes. The autolytic enzymes—the self-digesting enzymes—set free the chromogen groups of the proteid molecule, and these are oxidized by tyrosinase and converted into melanin after the

result has taken up iron and sulphur compounds. Gessard, after working with the enzyme isolated from plants, turned his attention to the melanotic tumours of grey horses, and came to the conclusion that the colour of the new growths is due to an oxidizing diastase acting upon some chromogenic agent, and that the pigment contains tyrosinase and tyrosin.

Perhaps one of the most suggestive, as it is one of the most interesting, researches upon the enzyme tryrosinase is that of Miss Durham (*Proceedings of the Royal Society*, 74, p. 310). She has shown that tyrosinase is present in the skin of fœtal and new-born rats and rabbits. An aqueous extract of the ground-up skin, when mixed with a solution of tyrosin and a drop of ferrous sulphate added to activate the solution, gradually takes on a dark colour, and a dark precipitate falls.

Artificial melanin may be obtained by heating together proteids and strong hydrochloric acid. A dark-brown material is obtained, and this is said to resemble in elementary composition and general properties the natural melanins, and when decomposed by strong alkalies to yield skatol, indol, and pyrrol derivatives, as do the natural melanins.

It has been shown also by Halle that under the influence of an enzyme, tyrosine is converted in the adrenal gland into adrenalin. When the adrenal is insufficient, as in tuberculosis of the adrenal, then in the human subject bronzing of the skin occurs (Addison's disease), and it is suggested that this bronzing of the skin is due to the tyrosin not being converted by the enzyme of the adrenal into adrenalin, but allowed to escape, accumulate in the tissues, and undergo change and the formation of pigment in superficial parts. The greater pigmentation of the exposed parts has been explained by the more active oxidation occurring in these parts.

Melanosis, as in the melanotic fibromata, appears to choose among equines the greys for preference, but melanotic fibromata may be found in other colours, though not commonly. In bovines the melanotic fibromata are most frequently seen in red and roan cattle, less often, even rarely, in what are called white cattle. As to why all horses and all bovines are not equally susceptible no explanation is offered, but in equines it should not be forgotten that the condition is observed in old animals rapidly whitening. The loss of colour from the hair throws a great amount of melanin into the body, and this is not converted for some reason into the colourless melanogen, but retained in the tissues, and most markedly in these new growths. An interesting point to clear up will be the relation of the cells bearing the pigment to the new growths. Are these cells the cause of the new growths, the development of the fibrous tissue in the so-called melanotic fibromata? Do they bear the relation of cause to effect? Are the fibromata, in other words, the response of the tissues to the creation of the chromatophores, the pigment-bearing cells? The bleaching of the hairs upon the integument of animals, as upon our own heads, is due to certain large cells, which Metchnikoff believes to be of epithelial origin, pigmentophages which rob the hair of its pigment and then return to the hair papilla, and then perhaps into the corium. But where the cell next goes we do not know, nor what is done with the pigment. Under ordinary conditions it is probably

changed into the colourless melanogen and excreted; in other cases, if the enzyme necessary for the conversion is absent, it may be stored. As Adami puts it, "it may well be that the extraordinary deposit of melanin in melanotic tumours, far from being a progressive acquirement, indicates a deficiency in the disintegrative mechanisms of the cell, whereby the normal final stage of colourless chromogen formation, or of protein disintegration, is not reached."

SPECIFIC CHRONIC ENTERITIS OF CATTLE (JOHNE'S DISEASE).[1]

I. By Dr. B. Bang, Professor in the Veterinary College, Copenhagen.

After a summary of the existing literature, which proves that this disease, unknown a few years ago, is spread over many countries of Europe and North America, Professor Bang gives a description of the pathological alterations, the symptoms, and the process of this disease, based on his own numerous researches.

His description of the pathological alterations are, in the main, similar to those that were known before. He draws, however, attention to the fact, that, as a rule, the covering of the epithelium is found to be intact, when immediately after the animal has been killed the bowels are fixed in a solution of formol. The desquamation of the epithelium and the necrotic appearance of the villi, formerly described by him, are only a cadaverous alteration occurring very soon. Then the writer points out that the pathological alterations, both the macroscopic ones and those that are only to be discovered by means of the microscope, are developed in varying degrees, and that even in cases in which the symptoms of the disease had been very important, occasionally a very trifling thickening of the mucous membrane, and, by means of the microscope, only a very slight infiltration with the peculiar epithelioid cells and giant cells can be observed. The number of the acid-fast bacilli lying in the cells is likewise very different, sometimes exceedingly great, so that the fuchsin-stained preparations assume a deep red colour; sometimes the number is so small that it is difficult to discover any bacilli. On account of this difference occasionally existing between the symptoms and the *post-mortem* examination, the writer supposes that a sort of poisoning plays a more or less important part in the process of this disease.

With regard to the symptoms the writer points out the fact that the evacuation of the bowels often during a very long period—in very exceptional cases during the entire process of the disease—can be tolerably natural. Emaciation and a small produce of milk in spite of great appetite are then the essential symptoms. As a rule, however, the animals suffer periodically from serious diarrhœa.

The process is, as a rule, a very slow one, so that the disease showing alternately changes for the better and for the worse can last for months; and even years. Calving often causes a change for the worse and the animals die then after a few weeks.

As a rule the prognosis is bad. The periods of convalescence can

[1] Summary of Papers presented at the International Veterinary Congress at The Hague, 1909.

last very long and apparently lead to recovery of health again. It is, however, very rare that a decided recovery follows.

Medicinal treatment seems to have only a transitory influence; on account of the spontaneous recovery that occurs so often, it is difficult to judge about the value of the treatment.

Etiology.—Professor Bang could not cultivate the bacilli that doubtless cause the disease. Experiments of inoculation on smaller animals as a rule proved unsuccessful; sometimes guinea-pigs and rabbits showed small abscesses. Only two out of the fourteen cows that provided inoculation matter could cause tuberculosis to some guinea-pigs, one rabbit, and two calves. Both cows came from tuberculous herds, and might, consequently, be bearers of latent tubercle bacilli. One of them had, moreover, trifling but distinct tuberculous nodules in some lymphatic glands. On account of these experiments in connection with the observation that the disease occurs chiefly among neats that do not show tubercle in reaction, that are found free from tuberculosis at *post-mortem* examination, and descend from herds that are free from tuberculosis, and that the disease is widely spread in the Isle of Jersey, where bovine tuberculosis is almost unknown, the writer (as likewise most enteritis experimentalists) is of opinion that the disease is in no way whatever connected with tuberculosis. The pathological alterations differ likewise by the special localization, the absence of ulceration and caseation from the usual tuberculous alterations.

According to Bang it is a specific contagious disease. Whether it spreads only from animal to animal by contamination of the food by the bacilli evacuated with the excrements, or whether the infection can likewise be caused by saprophytic bacilli, cannot be decided at the present moment.

The prophylaxis of the disease requires the isolation of the diseased animals as soon as possible. A speedy diagnosis was up till now impossible. In this respect it is of great importance that the reporter's co-operator, Mr. O. Bang, has succeeded in finding an apparently trustworthy diagnostic expedient in the tuberculin prepared from tubercle bacilli of birds. Subcutaneous inoculations with this avian tuberculin have occasioned in three herds of cattle free from tuberculosis, but suffering considerably from enteritis, distinct reactions, to about 33 per cent. of the grown-up neats. In the reporter's opinion one would not be justified in drawing from the power of reaction against a certain sort of tuberculin any other conclusion than this, that there must be some relationship between tubercle bacilli and enteritis bacilli.

II. By E. Liénaux, Professor in the State Veterinary School of Cureghem, Brussels.

(Translation by Dr. A. Liautard, Paris.)

The name diffuse hypertrophied enteritis of cattle is better than that of specific chronic enteritis. It indicates that the lesions are very extensive, and that the mucous membrane is hypertrophied, and distinguishes it from other specific chronic enterites.

The diseased mucous membrane is considerably thickened and shrunk; the mesenteric lymphatic glands are pigmented, tumefied, and

juicy. There are no tubercles. With the microscope it looks like lymphangitis of the mucous coat, sub-mucous layer, and of the glands; the lymphatic vessels are obliterated by granular tissue with epithelioid and giant cells. Some of them drop into the cavity of the intestines, and masses of bacilli are detected in the fæces. The aspect of the bacilli in bunchy masses has more value in the diagnosis than the shortness of the bacilli themselves, as the author has met with a case where they had the ordinary dimensions of the tuberculous bacillus.

Animals do not react to the test of tuberculin, because of being emaciated.

It has been said that it was not tuberculosis, because cultures of the bacilli of the special enteritis have not been made. But the disease is inoculable to guinea-pigs (mild lesions in the first series, generalized by reinoculation) to cattle and sheep. The bacilli of enteritis inoculated to cattle give them a noticeable resistance against tuberculosis inoculated afterwards.

The author concludes that the disease is a peculiar form of bovine tuberculosis, and he thinks that the bacilli that cause it may be a saprophytic variety of the bovine bacillus.

III. By Dr. W. Stuurman, Director of the Municipal Abattoir of Alkmaar.

(Translation by Dr. A. Liautard, Paris.)

Not agreeing with the negative results obtained by other experimentators in their attempts to cultivate the bacillus of the hypertrophying enteritis of cattle, I have undertaken experiments and succeeded in obtaining positive results; that is to say, that I succeeded in two cases in cultivating acido-resisting bacilli in the body of a rabbit and that of a guinea-pig which had been infected with products taken from cows affected with specific enteritis.

My first experiments, dating from 1904, were made in the abattoir of Leyden, of which Professor De Jong is director.

It was a very thin cow, which had excessive chronic diarrhœa, and which at autopsy proved to be affected with specific hypertrophying enteritis with the ordinary alterations, without any lesion of ordinary tuberculosis. Acido-resisting bacilli were found in masses or isolated in the mucus of the intestine, and in the mesenteric glands.

During six consecutive days a rabbit received in its food products from the scraping of the intestine and from the mesenteric glands. This infected food was eaten in large quantity.

Killed after eight and a half months the animal presented at the autopsy one caseous purulent nodule as big as a pea in the small intestine, and a large number of tubercles, softened in the centre, in the cæcum. The bacteriological examination revealed in these alterations several samples of acido-resisting bacilli. I have succeeded in cultivating and isolating from the pus of the nodule and from the small pearls of softened substance occupying the centre of the tubercles of the cæcum a very short acido-resisting bacillus, which judging from its growth in the media, and also of its pathological characters, is a bacillus of avian tuberculosis.

With this isolated bacillus I have experimented upon rabbits, guinea-pigs, white mice, fowls, and even on goats and on a calf. Up to the present time my experiments have failed in promoting the characteristic alterations of this disease.

The second case was discovered July 23, 1908, in the abattoir of Alkmaar. A cow, aged 4, much emaciated, was suffering with hypertrophying enteritis, and presented at the autopsy the typical lesions of the disease. Ordinary tuberculosis was completely absent. In the mucous membrane of the intestine and in the mesenteric glands many acido-resisting bacilli, gathered in masses or isolated, were found. Three guinea-pigs, five rabbits, two roosters, and a few white mice were infected through the digestive apparatus, under the skin, and in the abdomen, with products of scraping from the intestine and the mesenteric glands. After one and a half and eight and a half months the guinea-pigs and the rabbits were killed and presented various lesions. I succeeded again in cultivating from one of the guinea-pigs an acido-resisting bacillus. This guinea-pig had for six days eaten a large quantity of products from scrapings of the intestine, and besides had received under the skin of the right thigh a small piece of mesenteric gland from the cow. Killed after forty-nine days the right inguinal gland was swollen and contained caseous pus, the liver looked somewhat as in ordinary tuberculosis, the spleen was enlarged, the mesenteric glands were also swollen, and contained a little pus. Bacteriological examination was positive. Culture of the bacillus was positive with the product from the right inguinal gland, and the liver. The cultures were soft, and of the avian tubercle bacillus type. A very important point is to know, if in the two cases just described, we had to deal with spontaneous avian tuberculosis in the rabbit and in the guinea-pig, or if it must be admitted that we have succeeded in cultivating the bacillus of specific enteritis. The supposition that it is spontaneous tuberculosis is not admissible, specially with the guinea-pig. In this case the culture has succeeded also at the place of subcutaneous inoculation (inguinal gland.) Therefore it is very likely that specific hypertrophying enteritis is of tuberculous nature, due to a bacillus identical to that of avian tuberculosis. At any rate there are several facts, otherwise inexplicable, which are favourable to this conclusion.

In accordance with the results of my researches, and considering the contagious character of the disease, it must be recommended with a view to prophylaxis, to take the same measures as in cases of open ordinary tuberculosis—namely, to isolate diseased animals, and when the diagnosis is certain to kill them immediately.

IV. By Dr. Miessner, Professor, Chief of Laboratory in the Kaiser Wilhelm Institute for Agriculture at Bromberg.

The disease attacks cows at the age of from 3 to 6 years. Symptoms of the disease are a sudden diminution of the produce of milk, diarrhœa, and serious emaciation. At the *post-mortem* examination usually thickening and formation of corrugations of the mucous membrane of the bowels and swelling of the lymphatic knots of the mesenteric glands are discovered. The *Bacillus enteritidis infectiosæ*, which is not identical with the tubercle bacillus, must be regarded as the exciting cause.

Cows suffering from enteritis infectiosa do not react to tuberculin.

The *B. enteritidis infectiosæ* cannot be cultivated on the usual media. It is not pathogenic for the small experimental animals, especially for guinea-pigs and birds.

Calves can be infected with enteritis infectiosa by intravenous injection, or by feeding them with the mucous membrane of the bowels, or the lymphatic knots of the mesenteric glands of affected cows.

The milk of affected cows does not transfer the disease to calves.

The dung of cows suffering from enteritis infectiosa must be regarded as the source of infection.

As means of prevention we recommend: separation of the cows that have just been taken to the stable, from the old ones, and eventually, subcutaneous inoculation with an emulsion of lymphatic tubercles of suffering cows.

If the diagnosis is not sufficiently reliable and offers doubtful results, there may be the question of sarcoma of the bowels.

V. By Dr. H. Markus, Professor of the State Veterinary School of Utrecht.

(Translation by Dr. Liautard, Paris.)

The nature of the acido-resisting bacillus of specific chronic enteritis of bovines is a very important question, not only to the scientific point of view alone, but also in relation to hygiene. Indeed, the excessive abundance of the bacilli during the disease exposes the ground of the stables, the bedding, the people that handle the milk, the tools used for it, and the milk itself to become contaminated by the microbes contained in the fæces.

Liénaux, van den Eeckhout, and Bongert consider the disease as tuberculosis, and as being caused by bovine tuberculous bacilli of diminished virulency. Liénaux thinks he recognizes in this bacillus the initial stage of the saprophytic life of the tubercle bacilli of bovines. Bang, McFadyean, Leclainche, and Meyer do not accept the tuberculous character, Bugge and Cordsen prefer to wait for new researches. Nevertheless, Bugge, in collaboration with Albien, has cultivated the bacillus with the result, from his first communications, that the culture pleads against the tuberculous character. Pearson, whose work I have not been able to read in the original, appears not to consider the disease as tuberculosis.

Since 1904 I have been able to observe only two cases; with one only I made experiments upon animals. Several dozen tubes of culture media of serum-glycerine and glycerined potatoes, inoculated with the substance of a mesenteric gland, remained sterile, even after being kept several months in the thermostat. Six guinea-pigs and two rabbits remained perfectly healthy after being inoculated subcutaneously and also one rabbit and a hen which had been fed with the mucous membrane of the intestines.

If the bacillus that Stuurman has isolated from an experimental rabbit is truly the bacillus of enteritis, one must admit the researches of Koch and Rabinowitsch that it is an avian tubercle bacillus, and then that enteritis is produced by an infection of bovines with tuberculous bacilli of birds. The following plead *a priori* against this theory: (*a*) the refusal of the bacillus of enteritis to grow upon ordinary media containing glycerine, while the avian tubercle bacillus develops easily in primary culture; (*b*) that fowls cannot be infected *per os*, while the surest method to render fowls tuberculous is by the administration *per os* of avian tubercle bacilli. On the other hand, the results of *post mortem* of guinea pigs and rabbits inoculated with enteritic matter (Liénaux and van den Eeckhout, Borgeaud, Bongert, Bang,

Meyer, Markus) are negative — encysted abscess at the point of inoculation; small caseous and suppurating projections in the reticulum, the liver, spleen, mesentery, peritoneum, lymphatic glands of the mesentery and liver, the lungs; emaciation with enlargement of the spleen; general tuberculosis—and have much analogy with the results obtained on these animals by Koch and Rabinowitsch with matter and culture from tuberculosis of fowls.

The avirulency of the bacilli of enteritis for fowls is perhaps due to the passage during years of tuberculous bacilli of birds through the organism of mammalia, which in this case are bovines. Cadiot, Gilbert, and Roger have seen a disposition of this kind of pathogenity for fowls after a passage of three years through guinea-pigs (mentioned by Koch-Rabinowitsch). The failure in the attempt to cultivate remains difficult to explain, unless an influence of sojourn in the bovine organism is admitted; influence which removes entirely the ability of growing upon an ordinary medium containing glycerine.

What Bugge and Albien have provisionally mentioned is very important on this point. They have obtained cultures from mesenteric glands which prove against tuberculosis; thirty-two days after being inoculated with these cultures guinea-pigs were still healthy. Although this does not plead peremptorily against tuberculosis being caused by bacilli of birds, it is, however, necessary to wait with great interest the later details, which we are promised, concerning the medium of culture, the biology of the bacillus, and the experiments made upon animals with cultures.

With Liénaux I see in the fact—that after a more or less completely successful infection with material from enteritis upon guinea-pigs or rabbits (Bang, Bongert, and Liénaux), the inoculations of animals of the same species have failed—a powerful argument against the opinions of Bang, Leclainche, McFadyean, and Meyer, who consider that the phenomena that has taken place in animals of experimentation had probably been caused by bacilli of bovine tuberculosis, which were accidentally in the enteritic matter. If this opinion were right, the guinea-pigs, at least, still inoculated, ought to have become tuberculous, and it is astonishing that the symptoms had taken such limited extent in the inoculated animals in the first place. If there are here truly bovine bacilli of tuberculosis, it must be admitted with Liénaux and Bongert that their virulency is very diminished.

For me, the problem of the specific chronic enteritis of bovines is not ripe to allow the expression of a positive solution. This solution will only be possible after the study of the acido-resisting bacillus under all points of view, specially experimentally, cultivated without mixture, in several series, coming from various morbid cases. These are the experiments upon animals, made with pure cultures of the bacillus of enteritis, which will settle the question between *morbus sui generis* and tuberculosis, and if tuberculosis, between its bovine and its avian origin.

VI. By Mr. J. Bongert, Director of the Bacteriological Laboratory of the Municipal Abattoir at Berlin.

Specific chronic enteritis of cattle is much more widely spread than was hitherto supposed. It must be regarded as an infectious disease of the intestines, that is caused by a little acido-resistant bacillus,

found in prodigious quantities in the intestinal mucus or the mucous membrane of the intestines.

The clinical symptoms of chronic enteritis are a chronic incurable diarrhœa, causing progressive anæmia and emaciation. In decided cases the disease is considered incurable. Apparently pregnancy has an unfavourable influence on the process of the disease. The pathological and anatomical symptoms of the disease are very important—thickening of and formation of folds in the mucous membrane of the smaller intestines, caused by a diffuse infiltration of epithelioid cells with one or more nuclei. Formation of knots and ulcerous changes in the mucous membrane of the intestines do not occur.

The diagnosis must be made in most cases by ascertaining, by means of the microscope, the presence of these little acido-resisting bacilli in the fæces.

The reporter thinks the question still undecided whether chronic enteritis is to be regarded as a special form of tuberculosis, conditioned by attenuated tubercle bacilli, or an infectious disease specially restricted to cattle. Though there is much to be said in favour of the latter opinion, the writer thinks a positive decision on this point only possible when bacteriologists will have succeeded in making a pure culture of the acido-resistant bacillary agent, and they will be consequently able to repeat the experiments of infection, which have hitherto produced contradictory results, with pure cultures of the bacilli.

It may, however, be regarded as positively proved, that the supposition, hitherto generally entertained, that this infectious disease of the intestines of cattle can be caused by an infection with avian tubercle bacilli, must be regarded as fallacious, as the experiments of infecting hens and pigeons with intestinal mucus or mucous membrane of the intestines have decidedly failed.

As enteritis specifica of cattle is so widely spread, and this infectious disease causes comparatively such great economical losses, the writer thinks that the sanitary authorities should take the required measures to fight it.

THE ETIOLOGY AND PATHOGENY OF MALIGNANT NEW GROWTHS, ESPECIALLY OF CANCER.[1]

BY DR. E. F. BASHFORD, DIRECTOR, IMPERIAL CANCER RESEARCH FUND, LONDON.

ALTHOUGH the successful systematic application of the comparative and experimental methods to the study of cancer[2] is advancing our knowledge, the time has not come for propounding with confidence any new generalization on the etiology of malignant new growths. The meagreness of our positive knowledge on their etiology remains so constant that, but for the fact of its being the title officially assigned to this report, I should have refrained in the

[1] Part of a paper presented to the Ninth International Veterinary Congress at The Hague, September, 1909.

[2] The term "cancer" is employed as covering all forms of malignant new growths of epithelial and connective tissue origin, in keeping with the usage of the word in the English language. The investigations cover not only all forms of malignant new growths but also all forms of benign new growths.

present, as in the past, from using it as a heading to any account of the results of recent inquiry!

In the first place, the mere rapidity with which new facts—not necessarily bearing directly on etiology—are being brought to light by a large number of investigators, under the incentive of distinct working hypotheses, and the specialized nature of the observations that must be made at the present time, give cause for caution. It appears as unwise to under estimate the importance of the positive achievements attained under the ægis of the several older hypotheses as it would be lacking in perspicacity to attach exaggerated importance to newer working hypotheses formed under the influence of experimental research. The technical difficulties faced in the attempt to apply the experimental method are scarcely overcome. Only tardily have human pathologists conceded the importance of recent experiment, and of the many analogies between cancer in man and, *e.g.*, in the mouse. There are still too many gaps between the few positive facts to set up a claim to permanency for fresh speculations on etiology. With a few exceptions a direct attempt to explain the cause of cancer has been disavowed, investigators having preferred an indirect form of attack, *e.g.*, a study of how the cancer-cell grows, as in our case, which also implies a finer biological analysis of the properties of the cancer-cell, and of its relations to organisms. Indeed, we are still unable to produce cancer at will; it is possible that the study of etiology will not be pursued quite satisfactorily so long as this incapacity remains. In the second place, the results of recent inquiries are more destructive, as yet, of some older opinions while confirmatory of others, than productive of fresh and revolutionary conceptions. Still, a more precise definition of the direction in which the cause or causes of cancer must be sought is now possible. If I have little to contribute that is new to our knowledge of actual causation, I can put before you facts with which any generalization explanatory of the etiology of cancer must be in accord, and also I can put before you facts dismissing from further consideration alternative hypotheses of causation, which could be neither proved nor disproved so long as investigation was limited to clinical, pathological, histological, and statistical methods, without the final alternative of resorting to experimental tests.

The experimental studies of the Imperial Cancer Research differ from similar investigations on account of their wider comparative basis. They have been carried out on large numbers of different domesticated animals as part of the systematic investigation of cancer in all races of mankind and in vertebrate animals. Our investigations have disposed of the fiction that many races of mankind are exempt. Carcinoma and sarcoma occur congenitally in savage races of man, remote from the influences of civilization; and where the disease was said to be rare, *e.g.*, in Japan, we found excellent statistics of which Europeans were previously ignorant, proving cancer among the Japanese to be probably as frequent as among Englishmen and Germans. Taking another example, in Indian hospitals certain forms of cancer very common in London hospitals, *e.g.*, carcinoma of the lip, tongue, cheek, breast, uterus, are probably not less common in hospitals throughout Hindustan. In the case of most aboriginal races there are insurmountable difficulties in the way of even thus roughly

estimating its frequency among them. Therefore it is idle to affirm or to deny that cancer may be more common in some races than in others.

Our investigations have brought to light no indication of the endemic or epidemic occurrence of malignant new growths in savage races, nor has it been possible to establish any relation between the frequency with which cancer is recorded in aboriginal races and the degree of exposure to contact with Europeans. There is nothing comparable to the aggravated and fatal epidemics following the introduction of infective disease into aboriginal races. In the case of animals, the greater recorded frequency of cancer in domesticated as compared with wild animals, appears to be due, as I pointed out in 1903, not to contact with man, but probably to the fact that man so provides for and protects them that they live long enough to attain their respective cancer ages. We have shown that carcinoma and sarcoma occur not only throughout the human race, but also throughout the other vertebrates. The similarities of the lesions characteristic of malignant new growths are best illustrated by a series of carcinomata of the skin from man to marine fish living in a state of nature. As regards invertebrate animals there is less certain evidence of the occurrence of malignant new growths. The view—together with all its subsidiary assumptions—that cancer is only a disease of European civilization, and of domesticated animals, must be finally discarded.

The main condition for discovering a considerable number of cases in civilized and savage man, and in mammals generally, is the examination of a sufficiently large number of adult and aged individuals. From this observation Murray and I advanced the general conclusion in 1903-4, that when considered *statistically*, cancer was a function of age, and when considered *biologically*, a function of senescence. Its "age-incidence" in man—the importance of which had been long recognized by accurate statisticians and ignored by most pathologists—revealed a law applicable to all vertebrates, whether life was short or long. The law of the "age-incidence" of cancer is of fundamental importance, and applies both to individual organisms and to the individual organs and tissues of any one species. An explanation of the nature and etiology of the disease must be in conformity with it. It must be distinctly pointed out that many aged individuals escape cancer. Cancer is not caused by old age, and senescence of tissues is not the causative factor, but only an endogenous predisposing factor.

Since no race of mankind is exempt, the association of cancer with forms of chronic irritation [1] having nothing in common beyond their liability to produce chronic ulceration, chronic inflammation, or prolonged attempts at repair, is a fact of more moment than any futile discussion of the relative liability of different races of mankind. Carcinoma of the skin of the abdomen is practically unknown in

[1] *e.g. Physical injury*, as in fracture of bone, or in "brand" cancer or the "horn core" of cattle, where squamous cell carcinoma develops at the root of the right horn to which a waggon is attached in India; *chemical*, as in paraffin, petroleum, arsenic, aniline, &c.; *radiant* or *actinic*, as in short clay pipe, the Kangri, X-ray, or where the skin over the shin-bones of locomotive drivers has been exposed for years to the direct action of heat; *infective*, as in bilharzia of the bladder, tubercle in old lupus scars; *Treponema pallidum* in keratosis linguæ; tapeworms as recorded by Borrel; chronic inflammation and ulceration of all kinds, &c.

Europe, yet it is most extraordinarily frequent in Kashmir, because the natives there wear next to the skin an oven containing burning charcoal. Carcinoma of the floor of the mouth is rare in European women, although not uncommon in men; but in Ceylon and India generally the women suffer to a high degree from carcinoma of the inside of the mouth. This is due to the chewing of betel-nut and the practice of sleeping with the plug in the mouth; in the course of time carcinoma develops at the site so irritated. Without elaborating instances it may be stated, in short, that the incidence of cancer on the surface of the body in different races of mankind is characterized, on the whole, not so much by innate racial peculiarities, or differences in climate, soil and diet, as determined by external irritants. These and many other differences in the incidence of cancer cannot be explained by developmental differences between civilized and savage man. Instances for other sites of the body need not be quoted; suffice it to say that if all forms of carcinoma are to be explained by postulating the existence and the intervention of "congenital germs," then, since the point of application, *e.g.*, to the skin, in the case of squamous-celled carcinoma, is of no moment, it must also be assumed that such germs are as uniformly distributed over the surface of the body of all vertebrates, in this particular instance, as the skin is itself. In consequence of the necessity for this assumption, the explanation becomes no explanation at all.

The study of the association of cancer with irritants demonstrates absolutely that the generalization of the idea of a congenital or embryonic origin, together with the pessimistic views engendered of it, are indefensible hypotheses. It will become evident later that this conclusion agrees with the results of experiments, notably with the constancy with which different carcinomata of the mamma maintain the individuality characteristic of their different biological behaviour, with the experimental production of sarcoma, with the property of cancer-cells to elicit a specific connective-tissue scaffolding during propagation, and with the specificity of the phenomena of resistance to the growth of cancer.

Now, although the investigation of cancer in different races of mankind has added to the significance of the well-known fact of its being often associated with chronic irritation, I must point out emphatically that I do not feel justified at present in assigning anything more than an indirect or mediate etiological significance to this or to other exogenous factors. The significance of chronic irritation is qualified by the fact of its not occasioning cancer in all individuals who subject, with equal intensity, identical parts of the body to chronic irritation with resulting chronic ulceration. We may have to entertain the possibility of several etiological factors—some external to the body, and some internal.

Notwithstanding the fact that congenital tumours form an insignificant proportion of the total number of malignant new growths, and manifestly diverge from the forms of cancer decimating the adult population above 35 years of age,[1] the association of carcinoma and sarcoma with developmental anomalies is often advanced as the

[1] Ninety-six per cent. of the deaths from cancer occur above 35, and the chances of ultimately dying from cancer are in England and Wales 1 in 11 for men and 1 in 7 for women, above the age of 35 years.

criterion by which the validity of any explanation of cancer in the normally developed adult organism must be judged. Their occurrence certainly speaks against the indispensable intervention of external irritants. Not only did the occurrence of such growths appear to admit of an extension of the hypothesis that cancer is of embryonic congenital origin, or due to a reversion of adult cells to an embryonic (histologically undifferentiated) condition, but their occurrence has been regarded as a proof of its truth.

The occurrence of cancer in embryonic and in fœtal tissue, or in "unused embryonic germs," is just as much a problem as its occurrence in adult tissue. Embryonic tissue *per se* is not cancerous, it is not endowed with unlimited powers of growth, and there is no reliable evidence that it is capable of producing malignant new growths on transplantation. As will be shown below, the application of the descriptive term "embryonic" to cancerous cells is a misnomer. Its employment is the result of an ignorant interpretation of superficial morphlogical resemblances not revealing fundamental biological similarities, but deceiving those who have sought for embryological explanations; its use is due merely to the fact that histological and morphological methods did not enable earlier investigators to distinguish between "embryonic" and "histologically undifferentiated" cancerous cells with the demonstrative clearness characteristic of experimental methods. The cancer-cells differ biologically in many ways from the immediate descendants of the fertilized ovum, which alone possess powers of growth superficially resembling yet fundamentally different from those of the cancer-cell.

In considering the etiology of cancer regard must be paid to the sites of predilection in man and in animals. In England, among males, the organ most frequently invaded is the stomach; it is the seat of the disease in nearly 22 per cent. of the fatal cases, the liver and gall-bladder are invaded in nearly 13 per cent. of the whole, the rectum in 10 per cent., and the intestines in 8 per cent. Taken together the parts here specified are attacked in more than two-fifths of the total cases. Among females the generative and mammary organs are affected in more than two-fifths of the total cases; while further two-fifths are contributed by the stomach, liver, intestines and rectum, taken together. It is well known that cancer is more fatal to women than to men, and as well known that this fact is accounted for by the greater frequency by which the generative and mammary organs are attacked in women. In England and Wales in the seven years ending with 1907 the recorded deaths of males from malignant disease other than that of the generative and mammary organs were equal to a rate of 730 per million; whilst the deaths of females with the same reservation did not exceed 594 per million, the total deaths from all forms of cancer being 84,300 males and 122,964 for females. Therefore, when other individual organs are considered, there is an opposite contrast between the two sexes, *e.g.*, cancer of the lip, tongue, œsophagus, stomach and rectum is more common in men than in women, but in women cancer of the gall-bladder and liver is perhaps more common than in men. On the whole, the liability of males, both generally and for individual organs—excluding the generative and mammary organs—is greater than that of females, and it appears possible that the difference is due not merely, if at all, to constitutional con-

ditions determined by sex, but also by local circumstances peculiar to the organ attacked; perhaps by the customs of the two sexes, in the same way as the difference in the customs of women in India and in Europe determine their respective liability to and exemption from carcinoma of the mouth.

The predilection for some sites rather than others in mankind, and even the preponderance of certain forms of cancer in a single organ, *e.g.*, scirrhus carcinoma in the breast, however, must be considered also in the light of comparative investigation. In surveying the incidence of cancer in the vertebrate kingdom, one has been struck by the fact that certain forms appear to preponderate in different classes, *e.g.*, carcinoma of the thyroid in trout, of which we have records of almost 2,000 cases. It is, of course, obvious that the incidence of cancer in representatives of the different zoological classes must differ, since, *e.g.*, structures peculiar to mammals are absent in other vertebrates. But if we consider the mammalia themselves, it appears probable that some species are very liable to forms of cancer from which others, even nearly allied, are relatively or altogether exempt, as illustrated, *e.g.*, by the variations in the frequency with which the organs peculiar to the mammalia, the uterus and mamma, are attacked. Cancer of the uterus is rarely recorded in mammals other than man. Cancer of the breast, so common in the human female, is common also in the female mouse and female dog, but extremely rare in the cow, which, however, suffers quite frequently from squamous-celled carcinoma of the caruncle of the eye and from primary growths of the liver and adrenal, and these in turn are not so frequent in mankind. The carcinomata of the liver of the cow have a great tendency to form metastases in the lungs, with retention both of the typical structure of the liver and also of the bile-secreting function. Carcinoma of the liver is also common in the sheep. In mammals liable to carcinoma of the breast there are differences in the relation obtaining between the epithelial and connective tissue components of the tumour. These differences reveal themselves in the character of the connective tissue scaffolding; so that in the human female the scirrhus type is the common form of growth; in the mouse the stroma is usually very delicate. In the form of adeno-carcinoma which is most frequent there is a great tendency to the formation of dilated blood-sinuses and to hæmorrhages. In the dog there is a great tendency in the connective tissue scaffolding to the formation of bone and cartilage; in the rat to the formation of dense sclerotic tissue as in the human female. We meet with other idiosyncrasies, even in varieties of the same species, *e.g.*, in the greater liability of grey than of other horses to melanotic sarcoma.

The general homogeneity and the specific differences presented by malignant new growths in man and animals demonstrate the importance of regarding their etiology from the comparative standpoint. If infection can be excluded as the cause of the great frequency of cancer, intrinsic cellular properties acquire primordial etiological importance; but, from a general survey of the disease in man and animals, we have arrived at no definite conception of the relation of one case of cancer to another, whether in individuals of the same species or of different species, nor yet of the relation of tumour genesis, tumour growth, and tumour-bearing animals to one another. Although

we have recognized exogenous agencies and endogenous constitutional factors in the development of cancer, we have been unable to assign direct causative influence to any of them. Four positive comparative conclusions stand out. The first confirms that at which Waldeyer arrived in 1865 from his studies on man. The cells of the vertebrates, *e.g.*, of the normal covering of the body, possess or acquire some property or properties in common, in virtue of which they may be transformed into cancerous cells, under what appear to be very different circumstances. The second is the establishment on a comparative basis of the law of age-incidence. Third, experiment has demonstrated that the origin of the disease in a circumscribed area (Ribbert) is adequate to explain all the features of growth and dissemination, since they can be reproduced experimentally from a minute graft. Fourth, when all due weight is given to the significance of the circumstances of the transformation being concentrated on cells in a circumscribed area, the relations obtaining between these cells and the organism as a whole appear to be also of moment. Having got so far, the necessity for resort to experiment becomes acute.

Many tens of thousands of mice suffering with inoculated or spontaneous cancer have been under the most stringent observation in our laboratory. If cancer were communicable, animals housed along with those naturally suffering from or inoculated with cancer would be the first to suffer. In an experience extending over more than six years, *i.e.*, more than three times the average length of a mouse's life, exhaustive investigation has shown that this risk does not exist. This fact of itself satisfies those handling the animals. They incur still less risk in passing many hours daily dealing with cancerous animals in a room in which 10,000 of such mice and rats are usually housed at one time. If such a "cancer-house" as never before existed has no dangers to human beings who spend their days in it, *a fortiori* other persons have no ground for apprehension that cancer is communicable either directly or indirectly from animals to man. In corresponding observations on mice suffering from spontaneous cancer no case of transference from mouse to mouse has occurred.

We have frequently insisted that, in these respects, cancer presents marked contrasts to infective diseases, both to those which are naturally restricted to a genus, *e.g.*, syphilis, and to those which are so widely disseminated as cancer by being common to man and the whole vertebrate phylum, *e.g.*, tuberculosis. For, although no race of mankind is exempt, and cancer extends down the vertebrate scale to marine fish living in a state of nature, there are the most striking limitations to its communication from one individual to another. There is no connecting link, as it were, between the disease as it presents itself in nearly allied species nor even in individuals of the same species. There is nothing which, while foreign to the animal body, is nevertheless common to cancer wherever it occurs. There is nothing equivalent, *e.g.*, to the characteristics of syphilitic or tuberculous tissues which, no matter what the species of animal, are stamped with unmistakable common features by the presence of the *Treponema pallidum* or of the tubercle bacillus. The properties of the tubercle bacillus overshadow all the natural properties of the tissue containing it, and confer upon such tissue new properties essentially the same in all species of animals. Our observations lead us to

emphasize this difference in 1903-04, and repeatedly since. The distinctions of species and of the individual tissues of one and the same species are submerged in their acquirement of a new property, conferring on them the power of conveying the disease to previously healthy tissues, not only from one animal to another of the same species, but also to others of different species. The tuberculous tissues themselves, however, die when transferred to a new animal; they do not grow, they merely hand on the cause of the disease, viz., the bacteria, which continue to grow in new soil. It is not necessary to recapitulate the phenomena characteristic of the transmission of syphilis.

Alleged epidemics have been recorded in mice and rats housed together in small cages. Satisfactory proof that these aggregations of cases were due to infection has not been furnished, and not one of the exponents of infection has made allowance for the age-incidence of cancer. The alternative explanation that they arise as the result of inbreeding cancerous stock suggested itself. Our very detailed observations on many tens of thousands of mice have not revealed, in our laboratory, anything which we would call an epidemic.

Murray, Haaland, and I have devoted great attention to systematic breeding experiments, of which the starting point has been not merely mice of so-called cancerous stock, but mice which had also actually suffered from cancer. Thus the objection has been met of those who might argue that unless the disease had been present in the parent there was no opportunity for its transmission. The question of heredity of cancer of the mamma of the mouse, or of a predisposition to it, is now in a fair way to a final settlement. Experiments with the mouse have the great advantage that the life of this animal is short; many successive generations can be accurately observed, and age, dates of birth, and death, parentage, cause of death, and *post-mortem* examination fully recorded. In addition, a comparison with an average sample of the mouse population is possible. The surgical removal of spontaneously occurring mammary tumours, of which the clinical course and the pathological examination leave no doubt whatsoever that the tumours were malignant epithelial new growths, has enabled us to prolong the life of many mice and to breed from them. Breeding from such mice is not an easy matter, and much patience has been necessary. By successively crossing other spontaneously affected animals with the offspring of cancerous parents, strains are being obtained in which the cancerous heredity is half, three-quarters, or fifteen-sixteenths, and even higher. The concentration of a hypothetical hereditary factor in a known amount, and in large numbers of animals of known age should in the course of a few more years definitely settle whether there is a family or only an individual liability to the disease. In the first 400 female mice so obtained, which attained to an age of between 12 and 21 months, twenty-nine cases of carcinoma of the mamma occurred and no cases in other organs. It is important to note that this aggregation of cases of spontaneous cancer occurred notwithstanding the fact that the mice were periodically transferred to fresh and sterilized cages. The importance attached to prolonged sojourn in non-sterilized cages, by those who interpret this circumstance as evidence of infection, is thereby deprived of all significance. Thus far there is no evidence that the liability to carcinoma has been enhanced

by systematic inbreeding. I do not wish to anticipate the results of our observations, which are still continuing; but we have not as yet obtained an indication that cancer is inherited. It appears to be very doubtful whether there is transmitted even so much as either a constitutional or a local predisposition. Should this eventually turn out to be correct, there will be no alternative but to conclude that if local and constitutional conditions together are responsible for the inception of growth, then both can be acquired in keeping with the law of the age-incidence of the disease.

Our own systematic breeding experiments have yielded cases of carcinoma of the mamma in female mice in the following percentages: 6 to 9 months old, 2·2; 9 to 12 months, 3·5; 12 to 15 months, 7·4; 15 to 18 months, 14·2; 18 to 21 months, 33·3

All the facts recorded above, in so far as they have either direct or indirect bearings on etiology, are compatible with an endogenous origin of cancer, and the question now arises, has experiment given us any nearer insight either into the relations obtaining between tumours and the animals bearing them, or into the nature of the cellular problems hinted at? In both directions the results of experiment have become constructive and are becoming still more so.

There are facts so completely incompatible with the continued presence of an intracellular virus during the continued propagation of a tumour, as to make this conclusion appear no longer disputable, and the assumption of the presence of such a virus appears an unnecessary mental luxury. These are the facts relating to the changes actively induced in animals after inoculating, on the one hand, tumours of different species and of the same species, and, on the other hand, after inoculating the normal tissues of different species and of the same species. A sarcoma of a rat or a cat does not grow continuously when inoculated into a mouse, and such "vaccinations"[1] also lack the power to protect the mouse against the subsequent inoculation of a sarcoma, or a carcinoma of its own species. Similar negative results hold for corresponding "vaccinations" of carcinoma of strange species. Positive results, however, are obtained when mice or rats have been similarly "vaccinated" with carcinoma or sarcoma of their own species. These observations demonstrate that an intracellular virus has not conferred characteristic common properties upon the malignant new growths of different species, viz., properties depending upon it as the agent actively inducing protection. Further, as pointed out in 1906 by Murray, Cramer, and myself, and independently by Haaland, any particular tumour of a species induces protection against itself and others of its own kind better than it does against tumours of different kinds. The lesser degree of protection one kind of mouse tumour induces against others is due probably to its qualities *qua* mouse tissue and not to its properties *qua* cancer, for, it is of fundamental importance that mice and rats can also be protected by "vaccinating" them with the normal tissues of their own species, but not with the normal tissues of strange species. The degree of protection certain normal tissues induce corresponds closely to the relationship obtaining between the normal

[1] The word "vaccination" is used for convenience to indicate that the transplantation of tumour material had been unsuccessful in the first instance in that no progressively growing tumour resulted.

tissues vaccinated and the tumour subsequently implanted. Normal tissue may protect absolutely against the transplantation of an homologous tumour, *e.g.*, mamma against mammary carcinoma, or skin against squamous-celled carcinoma. These facts reinforce the significance of continuous growth of implanted tumours being restricted to animals of the species in which the tumours arose, and, together with this restriction, they make it unnecessary to assume that an intracellular virus is common to the malignant new growth of different species. They appear to make it equally superfluous to assume that an intracellular virus is either common to, or specific for, the several forms of malignant new growths of a species or even so much as common to the different kinds of malignant epithelial new growths occurring in one organ, *e.g.*, the mamma. From a review of the whole facts, one may indeed conclude that the malignant new growths of different species of animals resemble one another just as much, and differ just as much, as their respective organs and tissues do, *e.g.*, as much as the liver or the lungs of the mouse resemble and differ from the liver or the lungs of man. It also follows that cancerous tissues retain, essentially unaltered, both the tissue characters of a species and also the bio-chemical as well as the histological characters of the individual tissues of a species. The specific protection induced by differing malignant new growths demonstrates that malignant new growths do not possess the undifferentiated qualities of embryonic tissue. These conclusions are of fundamental importance in their bearing upon the etiology of carcinoma and sarcoma, and further, they are of far-reaching importance in the purely biological vista they open up. The exact quantitative methods we have employed, and the regard we have paid to several controlable factors—age of animal, doses, time intervals, &c.—influencing the results of transplantation, have led us to important conclusions differing essentially from those arrived at by Ehrlich, whose results, however, we have been able to obtain by employing adult mice and maximum doses for "vaccination" purposes. According to Ehrlich the protection induced by vaccinating the mouse with carcinoma or sarcoma of the mouse (the dose has not been published nor age of mice, and time intervals are not fully allowed for) is effective against all malignant new growths of that animal, vaccination with carcinoma protecting not only against other carcinomata, but also against sarcomata, and *vice versa*. Ehrlich's observations led him to set up the hypothesis of "pan-immunity" as between all the malignant new growths of the mouse, and in his most recent papers he quotes experiments of Schöne and Lewin, who claim to have induced resistance by vaccinating tumours of the rat and human species into mice, as evidence that "pan-immunity" may be capable of even wider extension. This doctrine excludes the specific nature of protection, not only as regards the tumours of a single species, but even as between those of different species, and if it does not concede it also does not exclude the possibility that protection (pan-immunity) may be induced by a virus common not only to carcinomata and sarcomata of the same species, but also the malignant new growths of animals so far removed as man and the mouse. Both these possibilities are absolutely excluded by the specificities of protection, revealed by employing the exact quantitative methods and the other precautions of our experimental procedure.

Any physical or chemical agency which robs a tumour of the rat or mouse of its power to grow in these animals robs it also of the power of inducing protection. The same agencies rob normal tissues also of their corresponding power to induce protection. Hypersensitiveness may follow the vaccination of tumour, or of normal tissue so injured; it is a phenomenon which may follow both the vaccination of fresh tumour tissue of the mouse, or of a different species, and the vaccination of fresh normal tissues of the same and of different species. Therefore it is not so specifically induced as protection.

Since 1903 I have often emphasized the importance of the fact that experimental propagation of cancer made the objective study of the growth of cancer possible. I have frequently emphasized the rational nature and the value of this study as an indirect way of approaching some etiological problems. The growth of carcinomata and sarcomata in animals previously normal has the advantage that both the growth itself and its consequences can be observed free from the complications and restrictions impeding their study in man, or in animals spontaneously attacked. The same malignant parenchyma can be studied for any length of time necessary. Thus it has been possible to prove that the presence of a tumour in a normal animal induces no effects referable to pathological products, toxines, or ferments directly injuring the animal. It has also become possible to substitute precise conceptions for vague speculations, such as that tumours "live at the expense of the organism," have "a higher avidity for foodstuffs," or "poison the organism with noxious products." The investigation of the metabolism of normal rats and mice bearing implanted tumours shows that it conforms to the normal. Observations made in our laboratory have demonstrated that it differs only in being quantitatively higher, in proportion to the amount of tumour tissue built up, as revealed by the study of the gaseous metabolism (Cramer) and the gastric secretion (Cramer, Copeman and Hake). The relation is similar to that obtaining between the fœtus in utero and the mother; but in the case of cancer, still greater masses of tissue are built up. Murray and I emphasized in 1904 the importance of the fact that the mere amount of growth obtained by propagating tumours was an entirely new biological phenomenon, worthy of investigation for the sake of its own importance. Later, having demonstrated that all the features of spontaneous cancer could be reproduced experimentally—local lesions, metastases, infiltrative growth, cachexia—by the continued growth of a few tumour cells successfully implanted, we concluded in 1905, from experimental observations made by Cramer, that mere growth accounted adequately for all the lesions and clinical features of the disease. Snbsequent systematic experiments made by ourselves and the later observations of others have fully confirmed this conclusion.

The immeasurable quantities of tissue elaborated during the growth of propagated tumours prove that more food is used up than the total required by all the animals bearing them. Experiments made in our laboratory have proved that individual animals are able, at least for a time, to supply the demands for food, but that ultimately the demand exceeds what can be supplied by a compensatorily enhanced digestive and respiratory activity, and without depriving the normal tissues of the organism of food. When ultimately the tumour comes to live at

the expense of the animal, death quickly ensues. It appears probable, at least for the tumours that have been investigated, that a constant ratio obtains between the maximum weights of tumours which can be borne without inconvenience and the weights of the animals supporting them. When the weight of tumour disturbs this ratio the animal at once suffers: age and other factors also modify the relationship. When very young animals are made to bear rapidly growing tumours they remain drawfs. The whole increase in weight the animals should show at a given age may be represented by tumour tissue. Somewhat older, but still growing animals, when similarly treated, show at a given age an increase in weight above that of controls of the same litter, and more than can be accounted for by the weight of tumour tissue. Hence it is possible under certain conditions to raise the supply of pabulum in the body fluids above the normal, and thus to compensate for the demands made for food by the tumour; but it must be noted that from this excess the normal cells of the body also benefit, so long as the gastro-intestinal tract keeps pace with the demand.

The growth of cancer, to which a natural limit appeared to be set by the death of the individual attacked, has been shown by propagation to be immeasurable. Its limitless growth is maintained by normal bipolar mitoses. Irregular forms of cell-division may occur, but they are not intercalated in the continuance of growth, nor is there any evidence of the intercalation of cell-conjugation. Cell-division is merely a consequence of continued growth of the living molecule: what requires explanation is not the ceaseless cell-division, but the ceaseless taking-up of nourishment and resulting growth of cells dividing by bipolar mitosis. The irregular forms of cell-division are but morphological manifestations of variations in the cell mechanism. Unlimited growth takes place in the same species only, because only there are the specific cellular foodstuffs purveyed from the intestinal canal, and, as will be stated below, the specific connective tissue and vascular mechanism proper to handing them on to the tumour obtainable.

Over eighty transplantable tumours of the mouse and rat have been studied in the laboratory. They include several representatives of the following groups: adeno-carcinoma, alveolar-carcinoma, adeno-carcinoma papilliferum, adeno-carcinoma hæmorrhagicum of the mamma, also squamous-celled carcinoma, adeno-carcinoma of sebaceous gland, spindle- and polymorph-celled and osteo-chondroid sarcoma. The different spontaneous tumours even of the same organ—the mamma—behaved differently at the primary transplantation into very large numbers of normal mice, and the majority have retained their peculiarities with slight variations during continued propagation. Therefore it seems probable, as pointed out by us in 1905, that at the time of transplantation they exhibited different forms of the cancerous and sarcomatous change. This would imply that the general biological features, acquired by the cells at the time when they undergo the transformation, are of a certain permanency, in keeping with the fact that during continued propagation—leaving out of consideration alternations in "growth-form"—the special features of growth and of histology may remain distinctive. Since in the great majority of the tumours we have studied there is neither a progress to a uniform

histological behaviour, nor advance to a uniform rate of growth and general biological behaviour, even in the case of tumours of one organ, the transformation of normal epithelial cells into cancer cells covers a whole series of modifications in the normal cell mechanism, one modification not necessarily advancing to another, *i.e.*, the interval of time not leading in every case to an augmented momentum as it were, till a final uniformity is reached. However, facts which necessitate caution in asserting such an apparent immutability, as applicable generally, also occur, and will be considered later on.

Jensen proved, and we confirmed and extended the observation to many other malignant new growths, that the tumours developing after the inoculation of tumour tissue arise from the continued growth of their characteristic parenchyma cells. All local and disseminated lesions follow from a small particle of tissue implanted into a normal animal. Cramer, Murray and myself showed that the local lesion of the disease, thus acquired experimentally, comes to have consequences parallel in every way to those following upon its spontaneous development in animals naturally attacked. Borrel and Haaland independently also worked out the details of dissemination by metastases. They are formed by the continued growth of the cancer-cells themselves. Therefore, the validity of conclusion drawn from study in man as emphasized by Ribbert, that the cancerous change occurs in a circumscribed area and grows from the constituent elements within the area affected and not necessarily through extension by apposition, has been established experimentally.

With Murray, I proved that the stroma is supplied afresh as a reaction of the connective tissues and blood-vessels of each successive host; the cancer cells have therefore not lost the habit of organoid growth. In the absence of these reactions tumours do not develop, *e.g.*, in highly protected animals, as shown by Russell's investigations, and also by Da Fano, who has found that the connective tissues respond not only locally but also generally throughout the body in the process of immunization. The connective-tissue scaffolding has specific characters for different tumours, even of the same organ and when nearly related histologically, and these characters remain constant. They are an expression of the specific innate chemiotactic properties of the cancer cells. This specificity proves that cells morphologically indistinguishable possess other distinctive features.

We have now advanced far enough into the study of cancer-growth to learn that vague explanations of its mechanism, *e.g.*, by assuming a retained or re-acquired "embryonic condition," the loss of "cell-equilibrium," "breach of organic continuity," are empty phrases for which more precise conceptions will ultimately be substituted. Von Hansemann has advanced the view that malignant growth arises in an "anaplastic" cell arising from an abnormal mitosis assigning too many or too few chromosomes to the daughter nuclei, and he has asserted that owing to a progressive loss of histological differentiation the metastases come to be less differentiated histologically than the primary tumour. The abnormal forms of cell division studied by von Hansemann are not intercalated in the continued growth of transplantable tumours, and to postulate the origin of cancer in an anaplastic cell seems to beg the question of origin altogether. It cannot be denied that the metastases of a tumour, *e.g.*, a squamous-celled carci-

noma, may be less differentiated histologically than the primary growth, but we have found in animals, as others have found in man, that they may be equally well and even more fully differentiated. In the subject of primary cancer it is impossible to decide what geneal-ogical or histological relation a metastasis has either to the differen-tiated or undifferentiated portions of a primary tumour. In prolonged propagation, however, the case is quite different; the study is then not limited by the brevity of life; an orderly sequence takes the place of the confused observations inseparable from the studies on the human subject. All such explanations have in common the fallacy that they assume far too simple a mechanism for the cell. The cell is really a very complex mechanism, our knowledge of which is being increased continuously, not only by the studies of a multitude of biologists interested in normal cytology, but also, as is perhaps less known, by experimental studies on cancer.

An unexpected phenomenon has been stumbled upon in the course of the propagation of carcinomata. Some of them have been replaced by connective-tissue tumours, sarcomata. There is no question of the conversion of epithelial into connective-tissue cells, and no question of an infective tumour. All the facts point to the acquisition of sarcomatous properties by what were previously normal connective-tissue cells, viz.: cells of the connective-tissue scaffolding, or stroma of the carcinomata. Since the stroma apparently degenerates, and is supplied afresh, as in other carcinomata that have not led to the development of sarcoma, the stroma was not possessed of malignant properties in the primary growths, and if this was the case then the cells of the normal connective-tissue of a new host or hosts must have acquired sarcomatous properties. In other words malignant new growths have been induced experimentally in previously normal animals. The nature and significance of this sarcomatous change are not yet finally elucidated. For the purposes of the present report it appears to me to be of moment that the circumstances under which this remarkable change has been effected are not identical. Ehrlich's cases developed in solid carcinomata of rapid growth, and giving high percentages of successful inoculations. Our cases, on the other hand, have developed in the first place in a very glandular-like adeno-carcinoma, tumour "37," which grows slowly and yields only about 50 per cent. of successful inoculations, and second in a hæmorrhagic adeno-carcinoma likewise of slow growth and moderate trans-plantability.

Tumour "100" is remarkable in that the sarcomatous change apparently takes place constantly after the transplantation of pure carcinoma, provided that progressive growth is maintained for from fifty to sixty days before the death of the animal. This sequence of events has been the invariable rule in the many instances of the phenomenon thus fully studied. The sarcomata have been either spindle- or polymorphous-celled. The areolas occurring in tumour "37" around the remains of the carcinoma are absent in tumour "100," which appears to resemble Ehrlich's cases in this respect. It has been possible to retain for both tumours "37" and "100," strains which still remain pure carcinomata.

In conclusion I should like to emphasize that no exaggerated importance is claimed for the working hypotheses put forth above on

the assumption that some experimental observations may be but a reproduction of what goes on in the body, although under the more intense exaggerated, influences of experimental conditions. It seems, however, permissible to push our reasoning from the processes observed in experiment back to the primary changes, and to infer that we have obtained a more precise conception of the mediate relation chronic irritation may have to the onset of cancer in the same way as the observations described on earlier pages appear to throw light on certain intracellular changes which, although only observed under experimental conditions, may be a reproduction of the changes responsible for the advance from a low to a high proliferative energy in the case of normal cells. I must point out emphatically that, at most, light is thrown only on the mediate or indirect relation of the irritant and not on the nature of the changed cellular mechanism ultimately responsible. The tendency, recently, has been to attempt to harmonize the apparent contradictions in the etiology and behaviour of malignant new growths, by assuming a "variety of causes" in place of the "single cause" of one or other sort, assumed in the several older hypotheses. Experiment has shown that harmony may be sought not so much, perhaps, in postulating a plurality of causes, as in fundamental common properties of living cells. We must, however, not forget that chronic irritation is only one of the conditions—and an exogenous one at that—inducing a change in environment and in this sense associated with the development of cancer. With no exact information as to the nature of the change from normal cell to cancer-cell, in which the ultimate explanation of the disease will be found, and as little exact knowledge of the endogenous factors (which certainly exist as pointed out in the early part of this paper), associated with the development of cancer, I refrain from discussing both.

At this early date it is sufficient to have thrown a little light on three aspects of the etiology of cancer. First on the constitutional conditions favourable and unfavourable for the growth of cancer-cells. Second, on how cancer-cells of low proliferative energy may re-acquire high powers of proliferation and of resistance to changes in their environment. Third on a possible nature of the indirect association irritants have to the disease, and equally on how some forms of cancer associated with chronic irritation may be avoided, for to my mind there is no doubt that Kangri cancer would cease to exist if the natives of Kashmir ceased to wear the Kangri, and cancer of the mouth in women in India would disappear with the disappearance of the habit of chewing betel-nut.

Experiment has put many older explanations out of court. I have illustrated how it is resolving the contradictions in the clinical behaviour and in the results of surgical treatment of cancer into orderly sequence. If experiment has not solved many of the old problems, it has replaced them by new ones, which is a fair proof that progress is being made. I have attempted to put forward some working hypotheses bearing on the possible relation both of the endogenous and the exogenous factors which play a part in the development of the disease.

Clinical Articles.

THE OPERATION FOR STRABISMUS IN A CASE OF DISLOCATED EYEBALL.

BY HENRY TAYLOR, F.R.C.V.S., HAYWARD'S HEATH, SUSSEX.

THE subject was a pug dog, about 10 years old, who injured his eyeball while being chased round a room by another dog, the eye coming in contact with a table leg. As a result of the impact the right eye protruded from its socket and was rotated in the horizontal plane from within to without. This condition gave the animal rather a repulsive appearance, or, to use the owner's expression, "the white was half over his eye." In other words, the internal half of the palpebral opening was entirely occupied by the sclerotic coat and the external half by the cornea.

The treatment first adopted consisted of fomentations coupled with pressure on the ball by means of the thumb, in the endeavour to gradually press it back into its socket, the pressure being renewed at frequent intervals. But Nature did not appear to be reducing the dislocation as quickly as one sometimes sees in cases like this; the ball remained protruding, the swelling did not diminish, and the rotation was as bad as ever. It was consequently decided to operate as for strabismus, and to suture the eyelids together and so produce a constant pressure.

Local anæsthesia was produced by the injection of approximately, 1 grain of cocaine in solution, under the skin of the outer canthus. The palpebral opening was then enlarged by slitting the outer angle, and the conjunctiva where it is reflected from the eyeball on to the eyelids divided in an upward and downward direction. A hook, extemporized by bending a very fine probe, was next inserted into the cavity, and then inserted between the external rectus muscle and the eyeball. This was rather a tedious item of the operation; there was only slight hæmorrhage, but the distance inwards rendered the finding of the muscle rather troublesome. After hooking the muscle its aponeurotic tendon was cut through with fine scissors, and a similar procedure was adopted with some of the fibres of the retractor oculi in that vicinity. The wound at the external angle was sutured and the lids were brought together by a suture in the middle.

The dog, practically speaking, never moved during the whole time. The sutures were removed in a few days' time and disclosed the fact that there was only a slight improvement. However, in a few days more a rapid improvement set in and the eye began to approach its natural position and appearance. Recovery was hastened by painting all round the eye with iodine which helped to disperse the swelling. The wound in the skin healed by first intention.

The final result of the operation greatly exceeded my expectations. One has to look very closely now to decide which eye was injured. There is one rather disappointing sequel which, however, has nothing to do with the operation; the eye is now amaurotic. This is no doubt due to the original stretching of the nerve and artery at the time of the protrusion.

THE USE OF ADRENALIN IN LAMINITIS.

BY R. A. PHILP, F.R.C.V.S., BRENTWOOD, ESSEX.

THE subject was a bay hunter gelding, aged 6. Before being properly conditioned he was given twenty miles fast work on a hard macadam road, and the next day he was unable to move. I was called in and found the horse affected with acute laminitis in his forefeet. I administered at once a 5 drachm physic ball, and prescribed fever draughts containing spts. ether, nit., and tinct. aconiti. Instead of improving, however, he gradually got worse and was quite unable to rise. I then had him slung for a short time twice daily for three days. By this time there was still no improvement; in fact the patient seemed even more distressed than before. He was in acute pain, and sweating profusely. His temperature was only a little over 102° F., but his pulse was over 80 per minute.

It was at this time that I determined to use adrenalin, so I mixed 1 drachm of adrenalin hydrochloride solution (1-1,000) with 3 drachms of normal saline solution, and injected 1 drachm of the mixture subcutaneously on each side of his fore fetlocks over the digital arteries. In a few moments the effect was little short of miraculous, the relief being very marked and very rapid. The blowing diminished, the pain was gone, and the animal was able to walk comparatively freely. The temperature subsided slightly and the pulse became normal. Unfortunately, however, the horse developed septic pneumonia a few days later, to which he eventually succumbed.

[The above case is certainly most interesting and instructive. There is every reason to believe that excellent results may be obtained from the use of adrenalin in early cases. The fact that Mr. Philp's case eventually died from septic complications in no way detracts from the usefulness of the adrenalin. Probably other practitioners will be constrained to use it, and we should be glad to receive accounts of their cases whether successful or not.—ED. *V. J.*]

CYST OF THE PROSTATE WITH ENLARGEMENT.

BY ARTHUR PAYNE, F.R.C.V.S., WEYBRIDGE.

THE subject of these notes was a collie dog, aged 8. I was consulted in October, 1907, as for some days he had experienced a difficulty in passing his urine. I found the patient looking very well, in good condition, lively, appetite good, pulse and temperature, &c., normal. The urine was not ejected with force, as under normal conditions, but issued in a dribbling stream. It was normal in appearance. No pain was evinced after its passage, and the dog frisked about quite happily.

I could find no traces of calculus in the urethra or bladder, and as I thought the symptoms pointed to hypertrophy of the prostate, I made a rectal examination, and readily detected an enlarged prostate. Urotropine, gr. v., was prescribed three times daily, and two days later the urine was passed without the slightest difficulty.

In September, 1908, I was again requested to call, as the symptoms of a year ago had returned. This attack lasted about five days, with apparent recovery after the same treatment.

On September 27, 1909, I received an urgent message requesting me to call as soon as possible. I found the patient lying down, and continually surveying the pelvic region with an anxious expression occasionally licking the skin covering the abdomen near the groin. I was told that for the last two or three days he had had a return of the old symptoms, but he appeared in very good spirits and had taken his food. We had the greatest difficulty in persuading him to stand, and when on his legs he stood with back arched and tail depressed, walking very stiffly, not bending his hind legs. A few drops of blood-stained urine came away, the passing of which seemed to cause him pain. I expected to find the bladder distended, but this was not the case; the explanation of this being, in my opinion, that the urine was more or less continuously coming away a few drops at a time.

An examination *per rectum* showed the prostate enlarged to such an extent that the rectum was pushed upwards. This enlargement rather puzzled me, as it was of such a yielding character, the nature of which did not strike me at the moment, although I recollected afterwards that I had once seen a similar *post-mortem* specimen at a Central Veterinary Association meeting. I recognized the futility of medical treatment, but prescribed urotropine and morphia.

On the 28th the only change worth recording was the ease with which the urine was voided; this occurred every time the animal stood up (which was fairly constant), and came away in quantities of 2 oz. to 3 oz. each time in a big stream and more or less involuntarily.

On the 30th the bowels were moved, after the administration of 3 gr. of calomel—1 gr. given every hour for three hours. He was decidedly weaker, his hind quarters swaying as he walked; appetite completely in abeyance and pulse very weak. From this day he steadily grew worse, and died a few days later.

The *post-mortem* examination showed that the prostate gland was enormously enlarged and cystic, the latter portion alone being quite the size of an ordinary orange, whilst the remainder of the structure was hardened and cirrhotic. The cyst contained a clear, straw-coloured fluid, about 4 oz.

MASTITIS IN COWS.

BY S. J. MOTTON, M.R.C.V.S., PENZANCE.

DURING the last few months in certain parts of West Cornwall many interesting cases of mastitis have occurred in cows. Although numerous, these cases appear not to be very contagious, for they have almost without exception been single, and no connection has been traced between one case and another. There is, however, a very close resemblance between them, and there would appear to be no reason to suspect that the causal organism in them all is not the same. Why so many similar cases arising sporadically should have made their appearance at the same time is not clear, unless one supposes that some climatic influence has this autumn been very favourable to the multiplication of the causal organism; for animals in the different stages of lactation have been affected, without any preference being shown for

those which have recently calved or cows which are in the process of "drying off," or which have been carelessly dried off.

As with most other forms of acute mastitis there is frequently much systemic disturbance, and the temperature is often 104° to 105° F Fatal cases are by no means rare. The onset is sometimes very rapid, and an apparently normal udder may, in twenty-four hours, become the seat of most intense inflammation. Usually, however, inflammation is at its height in from three to five days.

At first it is the rule for one quarter only to be affected, but ultimately two or even three quarters are not infrequently involved. The first symptoms in connection with the udder are heat and pain, together with a diminution—more or less marked—in the quantity of milk, which is also changed in colour. Frequently it resembles whey and contains clots; at other times it is sanguinolent. Gas formation may take place, and then when one draws out the quarter the feeling conveyed to the fingers is similar to that experienced when one milks out a quarter after the injection of gas in the treatment of milk fever. The udder, at first hot, painful, and œdematous, after a few days becomes harder and less painful; the skin darkens in places, the teat becomes doughy and cold to the touch, and it is now very difficult to draw through the teat, from the affected quarter, anything more than a little curd.

The skin in the places where it has become abnormally dark takes on a dry and leathery appearance, and on palpation one frequently finds that these areas are thinner than the surrounding skin. Here and there on their surface beads of moisture may be present, and it is often possible to thrust one's finger through the dead skin into the galactophorous sinus, when a custard-like material with a putrid odour escapes. In the majority of these cases we are justified in hoping, not so much that we shall save the quarter or quarters, but that we shall save the cow and permit the owner to convert her into beef.

As this mastitis in all probability starts in the milk sinus, it is obvious that treatment by means of the injection of antiseptic solutions will be most successful in those cases where it is commenced before the disease has extended far into the lactiferous canals and their numerous ramifications. In such cases the quarter may occasionally be saved, but usually we are not called in until the disease has become rather more advanced.

Cases treated in the ordinary way—viz., by frequently drawing out the affected quarter, by the application of some form of liniment and the administration of appropriate medicines internally, may, like others which are allowed to take their chance without any special treatment, recover, but the most successful treatment is apparently the injection of antiseptic solutions into the milk sinus. Good results often follow two injections of 2½ per cent. acid carbolic., with an interval of a few days between them.

It is probable that much more frequent injection of the solution is desirable (and one cannot help wondering at the success which follows two injections), but the country practitioner is often a long way from his case, and it is not always wise to leave the injection of the solution either to the owner or his cowman. The affected quarter should be first milked out and the solution injected, then drawn out and replaced, the second injection being allowed to remain in the quarter for two or three hours.

In conjunction with this, of course, frequent milking out is practised, the part rubbed with liniment, and any internal medicine considered necessary administered. When it is no longer possible to draw the contents of the sinus through the teat, the advisability of opening the sinus has to be considered. This may be done either by opening the teat longitudinally, by amputating it, or by opening the milk sinus with a knife in the place where, if left to itself, the pus usually breaks out—viz., where the skin becomes leathery at the base of the teat.

Such an incision results usually in the escape of much purulent custard-like material, and it is often possible, by inserting the finger into the opening and working it around, to dislodge a portion of dead mammary gland; in some cases the whole of one or two quarters may be removed in this way. Not infrequently the more or less dead mammary tissue comes away freely; sometimes it is held in position by strands of connective tissue and blood-vessels, which break as one pulls or twists at the loosened mass. It is usually three or four weeks, however, before very large masses can be so removed, and although as the vessels break through a hissing noise may be caused by the escaping blood, hæmorrhage usually soon ceases and is not serious.

Care must be taken when one opens the milk sinus with a knife. It is not advisable to risk this operation unless the skin at the part is nearly or quite lifeless. When the knife is used on tissues in this region, which are still well supplied with blood, considerable hæmorrhage may follow, and it is difficult to pick up the bleeding points. Should it become alarming it is well to insert a plug of hemp or cotton-wool and secure it with one or two sutures. These may be removed next day with safety.

In any case where the teat is opened or amputated, or where the sinus is opened, it is well to supply the owner with a glass male syringe and some antiseptic solution, by means of which he can safely wash ou the sinus. In from two to four weeks the udder shrinks, the wound closes, the animal begins to improve in condition, and may be converte into beef.

UNIVERSITY OF LONDON.

Award of University Scholarships and Medals.

The following award has been made upon the results of the Second Examination for Medical Degrees, Part II., July, 1909:—

University Scholarship in Pharmacology—Mr. Thomas Chivers Graves, M.R.C.V.S. (University College).

Abstract.

BILIARY FEVER OR MALIGNANT JAUNDICE OF THE DOG (CANINE PIROPLASMOSIS).[1]

BY WALTER JOWETT, F.R.C.V.S., D.V.H., VETERINARY BRANCH, CAPE TOWN.

The Drug Treatment.

The following observations relate to a method of treatment for canine piroplasmosis recently discovered and described by Professor Nuttall, of Cambridge University, and Dr. Hadwen, of the Health of Animals Branch, Department of Agriculture, Canada.

These two investigators found that the administration of a dye known as Trypanblau to dogs suffering from biliary fever, resulted in most instances in effecting a speedy cure.

This disease being a veritable canine scourge in the Cape Peninsula, and along the coastal area of the Colony and for some distance inland, it was decided to institute a series of experiments at the Rosebank Experimental Station, in order to verify this reported successful method of treatment as applied to the disease met with in the Cape, and also to ascertain its usefulness or otherwise in regard to certain other diseases of animals.

As a preliminary to the carrying out of these tests it was necessary to procure an animal (dog) actually suffering from the malady (canine piroplasmosis) in order that other canines might be infected therefrom. This was finally accomplished, an Irish terrier being handed to the writer in the last stages of the disease, and from this animal a series of dogs were infected by experimental blood inoculation. A number of the animals so infected, after manifesting symptoms of the disease quite apparent to the untrained observer, were placed under treatment and the result carefully noted, the remainder, a small proportion, after being infected with the malady in like manner, being left without treatment to act as controls. In addition to these animals, a few dog owners very kindly came forward with their sick dogs—animals which had contracted the disease under natural conditions, *i.e.*, by the bites of infected ticks; after verifying the presence of the causal agent of biliary fever in their blood by microscopical examination of that fluid, these also were placed under treatment.

Two of these last-mentioned animals unfortunately, when submitted for treatment, were almost *in extremis*.

Before proceeding further, it may be said that excepting for the two animals just mentioned—in which recovery was quite hopeless—the Trypanblau treatment proved an unqualified success, and our experiments entirely confirm those of Professor Nuttall and his co-worker.

When administered by subcutaneous or intravenous injection, Trypanblau speedily colours the tissues of the animal a more or less well-marked blue shade. This is naturally most noticeable in the case of white dogs, such as fox-terriers, and is most apparent on the inner aspect of the hind-legs, on the under surface of the abdomen, and on

[1] Contributed to the *Agricultural Journal of the Cape of Good Hope*.

the membrane lining the mouth and eyelids. The animal remains so coloured for some days, when the blue coloration gradually passes off, disappearing first from the membrane lining the mouth, and later from the skin covering the lower surface of the abdomen. The urine likewise assumes a blue colour.

In those subjects which die after undergoing treatment with this dye, it is found that practically all the tissues of the body are of a vivid blue tint.

On the causal organism of biliary fever the action of the dye is very marked. When injected into a dog obviously ill and harbouring many piroplasmata in its blood, no very noticeable change may be apparent for a time to the casual observer, excepting, of course, that the subject becomes coloured. If, however, one proceeds to examine the blood of such subject, it is found that the parasites therein present become less in number and in a few hours have totally disappeared. Associated with their disappearance there is invariably a fall in the body temperature, the animal may remain dull and listless and apparently ill for some twenty-four hours or so after the injection of the dye, this notwithstanding that its blood may be freed from parasites and the hyperthermia less marked; soon, however, the subject is appreciably better, it manifests a desire for food, and its recovery then in many instances is rapid and complete. True, some days afterwards, if the body temperature be recorded, periodic elevation will be noticed, but these do not seem to be associated with obvious signs of ill-health.

This is the state of affairs when an animal is submitted to the treatment before its condition has become hopeless. Here it may be said that in all our experiments treatment was not commenced until the subject was obviously ill—*i.e.*, until the casual observer could see that something was amiss with the animal. Some of the experimental animals indeed were seriously ill before being placed under treatment. In one or two instances hæmoglobinuria was a characteristic symptom, and yet such subjects recovered.

Needless to say in all the experimental animals the presence of the causal parasite of the disease was demonstrated in the blood prior to commencing treatment, and in all cases the results were controlled by microscopical examination, together with clinical observation and careful and regular thermometric readings.

Mode of Treatment.—The dye must be injected under the skin or directly into a vein. Administered by the mouth it exerts no beneficial effect whatever.

When injected under the skin it unfortunately gives rise in many instances to some local irritation, producing in certain cases considerable swelling at the point of injection, and occasionally abscess formation and sloughing of a small portion of skin; this, notwithstanding that all precautions may have been observed to prevent organismal contamination—careful sterilization of the syringe and needle used for injection, washing, and disinfection of the point of inoculation, &c.

On account of this disadvantageous feature, it is advisable whenever possible to inject the drug directly into the blood stream; by this means the action of the dye is speedily exerted, and one obviates entirely any possibility of the appearance of a troublesome

local swelling or abscess formation. With practice it is not a very difficult matter to inject the drug in this way directly into the vena saphena in the hind leg of a large or medium-sized dog. The operation is not so simple in a small, fat, woolly, and anæmic animal. If for any reason intravenous injection of the drug is impracticable, then the solution may be injected merely under the skin. True a swelling may form, and this may perhaps be troublesome; still this is of but little moment when compared with saving the animal's life.

A saturated aqueous solution of the dye may be injected either into the vein or under the skin; this is, roughly, a 3 per cent. solution. We have prepared this solution by adding a measured quantity of recently boiled water to a definite quantity of the dye, using the liquid when at blood heat. In some instances the solution has been boiled shortly before use, and we have not noticed any impairment of its action by this procedure. For small adult dogs and puppies a 1 per cent. solution should be injected subcutaneously. In very small animals where but little of the drug is introduced under the skin there may be but slight local swelling at the site of injection.

It is probably advisable, if not absolutely essential, to use a freshly prepared solution, and in the experiments recorded hereunder practically only such has been utilized; in but one or two instances had the solution been stored for some days prior to its injection.

The following is an abstract of the experiments conducted at the Rosebank Experimental Station:—

Experiment A.—Three dogs, all infected experimentally by injections of blood obtained from a naturally infected case immediately after death. The dose of blood injected subcutaneously was 1 cc.

No. 1.—Fox-terrier in good condition, weighing 13 lb. His temperature began to rise on the fifth day after inoculation, and piroplasms were demonstrated on the seventh day. By the ninth day he was obviously very ill, and refused food. He was injected with 5 c.c. saturated solution of Trypanblau subcutaneously. Fourteen hours later no piroplasms could be found in the blood, and his temperature began to subside. Recovery was ultimately complete and satisfactory, and by the thirty-sixth day after infection the dog had gained 2 lb. in weight (15 lb).

No. 2.—Irish terrier, weight 36 lb. Piroplasms present on eighth day. Obviously ill on the tenth day, when Trypanblau was injected subcutaneously. No piroplasms to be found next day. Recovery satisfactory and complete.

No. 3.—White terrier mongrel; fairly good condition. Piroplasms found on eighth day, and dog obviously ill. He was not treated and he died on the tenth day

Result of Experiment A.—Of the three dogs experimentally infected the two treated with one dose of Trypanblau promptly recovered, whilst the untreated control died.

Experiment B.—Two puppies experimentally infected by subcutaneous injection of 1 c.c. of virulent blood.

No. 4.—Aged 2 months and weighing 3½ lb. Became ill on the eighth day and worse on the ninth day, when he was injected subcutaneously with Trypanblau. He made an uninterrupted recovery.

No. 5.—Aged 2 months, weight 4 lb. Became ill on the seventh

day and got worse. He was not treated and was found dead on the eleventh day.

Result of Experiment B.—Of two puppies experimentally infected one was treated with Trypanblau and recovered, the other was untreated and died.

Experiment C was practically a repetition of Experiment B. Of two puppies (Nos. 6 and 7) infected one was treated and recovered, while the control died.

Experiment D.—On three dogs experimentally inoculated.

No. 8 was injected intravenously with bloody serum from No. 5 at death. Obviously ill on the fifth day, and piroplasms found. Treated with Trypanblau on the sixth day and recovered.

No. 9 was injected with similar material from No. 5, but subcutaneously. He showed no signs of illness on the third day, but was injected with Trypanblau to see if it might prevent the appearance of parasites. He did not become ill, and on repeated microscopic examination no parasites were found. An attempt to infect him will be made later to see if this experiment has conferred any immunity.

No. 10.—In this case the process was reversed. He was first injected subcutaneously with Trypanblau, and on the sixth day injected intravenously with 1 c.c. virulent blood. No piroplasms were ever found in his blood. It is unlikely that he has developed immunity, but that will be tested later.

Experiment E.—Three puppies inoculated with virulent blood, and all became infected.

No. 11 received on the fourth day 1 fluid ounce of Trypanblau saturated solution *by the mouth*. He was found dead on the sixth day.

No. 12 was injected intravenously with 5·5 c.c. Trypanblau solution, and recovered.

No. 13 was untreated and died on the tenth day.

Clinical Cases.—This group includes only animals which acquired the disease under natural conditions—*i.e.*, by means of infected ticks. The dogs here referred to were handed over for treatment when obviously very ill indeed; two, in fact, died soon after their admission. The remainder (four) were very well marked cases, and we fully believe that had they not received the Trypanblau treatment all these animals would have succumbed to the malady.

It is true that animals do occasionally recover from biliary fever, even in the absence of drug treatment. Such an occurrence, however, is far from common; in fact, we may go further and say that it is very rare indeed.

Comparing the experimentally induced disease (*i.e.*, that following the inoculation of virulent blood) with the naturally acquired one (that is by tick infection), we incline to the belief that the latter is the more severe and the one less frequently followed by recovery.

But to return to our four successfully treated clinical cases—the improvement has been maintained in every case; the recovery is complete. In one a relapse occurred on the seventeenth day after the injection of the dye; piroplasmata reappeared in the blood and the animal was very anæmic; nevertheless it remained quite lively and continued to feed much as usual. The disease, in fact, in this case, has assumed the chronic form, with few parasites in the blood. In this animal, as in the remainder of our naturally infected dogs, a sufficient

length of time has not yet elapsed to enable one to state with absolute certainty that the recovery will be permanent. We fully expect, however, that such will be the case.

Summary.

Experimental Cases.—Six dogs infected experimentally with biliary fever (by injection of virulent blood) and subsequently treated with one injection of Trypanblau—all recovered.

Four dogs injected in like manner, but which did not receive drug treatment—all died.

One experimentally infected dog, in which the treatment was attempted by the administration of a dose of Trypanblau *by the mouth* also succumbed.

One dog infected experimentally and injected three days later subcutaneously with half-dose of Trypanblau before parasites had appeared in its blood remained well; as did also an animal which received a dose of Trypanblau and six days later an injection of virulent blood.

Clinical Cases.—Two dogs in which treatment was attempted when moribund died.

Four dogs very ill and manifesting severe symptoms of biliary fever (red coloured urine, anæmia, yellow coloured membranes, &c.), under treatment by injection of Trypanblau—all recovered.

Immunity.—Immunity is known to follow recovery from the naturally acquired disease; and, in the case of dogs living in infected areas, this immunity is maintained and reinforced by the further repeated tick infection to which they are exposed. In the absence of this, it is doubtful whether the immunity of "salted" animals is of any considerable duration (*i.e.*, lasting for more than from one to two years). Throughout the duration of the period of insusceptibility it is known, of course, that the blood of the "recovered" dog is infective for "clean" ones, the same, whether it be inoculated into the latter experimentally with a syringe, or by means of the dog tick.

In regard to dogs which have recovered from an attack of biliary fever as a result of the "Trypanblau" treatment, it remains to be seen: (1) Whether the blood of such dogs is still infective on inoculation into susceptible canines; and (2) whether, after recovery from the disease in consequence of the Trypanblau treatment, the subject possesses an immunity against subsequent infection equal to that following the recovery which occasionally occurs without drug treatment.

It is expected that such will be the case,[1] and in the event of further experiments confirming this expectation, one would be in a position to immunize susceptible canines, by (1) infecting them with the disease, either by blood injection or by tick infestation, and (2) so modifying the resulting reaction by nursing and treatment that recovery would be assured; in other words, passing the subject through a mild form of the disease. Thereafter, the immunity of animals living in an infected region would be maintained by the periodic tick infestation to which they would naturally be exposed from time to time.

[1] Since the above was written the dog mentioned in the foregoing experiments (A, No. 1) has resisted an inoculation of virulent blood; he is now, therefore, evidently immune.

An endeavour will be made to elucidate these points by further experimental work, and for this purpose we intend to utilize the "recovered" dogs mentioned in the foregoing records, together with others. Some weeks and months hence, a number of these animals will be submitted to the attacks of infected ticks, whilst others will receive an injection of virulent blood. In this way it will be possible to ascertain the duration and degree of their immunity.

Whether or not these expectations be realized, the fact remains that the researches of Professor Nuttall and Veterinary Surgeon Hadwen have given us a successful method of curative treatment for the disease, canine biliary fever, a disease in regard to which all former methods of treatment proved ineffective.

Miscellaneous.

Mr. T. D. Young, M.R.C.V.S., who has been Chief Meat Inspector at the Deptford Foreign Cattle Market, has been appointed Meat Inspector at the Central Meat Market, Smithfield. Both professionally and personally, Mr. Young is eminently well fitted for his new post, which, by the way, is a new departure, since this is the first time the inspection at Smithfield is to be placed under veterinary supervision.

We regret to announce the death of Mr. James King, M.R.C.V.S., of the Metropolitan Cattle Market, Islington, whose portrait we reproduce as the frontispiece of this issue.

Our readers will be very sorry to hear of the death of Mr. Albert Wheatley, F.R.C.V.S., of Reading, which took place on Thursday, November 25.

Lieutenant-Colonel Appleton, A.V.D., has been elected a Fellow of the Royal Geographical Society.

Reviews.

Biological Albumen Differentiation Procedure, with Special Reference to the Forensic Examination of Blood and Meat, and the Obtaining of Precipitizing Sera. By Professor Dr. P. Uhlenhuth and Dr. O. Weidanz.

This is a German volume of 246 pages with thirty-eight figures in the text, published by the firm of Gustav Fischer, of Jena. It deals exhaustively with the effects occasioned by antisera on different kinds of blood. The precipitin reaction has been proved to be evident even in the material of mummies 3,000 to 5,000 years old. Incidentally, its useful side is shown in distinguishing the different kinds of milk (sheep's, goats', cows'). The biological method is not a specific blood proof, but a specific albumen reaction. An exact forensic examination of blood must be directed to (*a*) proving blood (*b*), the determination of the origin of blood.

The chemico-physical examination of the vital fluid includes testing by the ozone, capillary, benzidin methods and the spectroscope.

In criminal investigations and the determining of the character and source of different blood stains the biological reaction of albumen has been of inestimable value. It is based on the fact that serum of rabbits which have been inoculated with the blood of different species of animals precipitates solutions of the blood of these animals. Thus the sera of rabbits injected with man, pig, horse, cat, or cow blood give precipitates only with the vital fluid of human, porcine, equine, feline, and bovine subjects respectively.

Suspected stained articles of clothing worn by criminals, smeared objects near the scenes of their evil deeds, weapons of assault were sent from numerous parts of Germany for Dr. Uhlenhuth to examine.

The things comprised cudgels, cotton-wool, sand, stockings, tablecloths, chemises, waistcoats, vests, &c. Many of the investigations led to the discovery of human blood, but the circulatory fluid of pigs, fowls, deer, &c., was also encountered, and when found would, no doubt, frequently tell in favour of the suspected person. Accounts are given of forty experimental proofs of this nature and the methods adopted.

Conclusions based on them would seem to have been very satisfactory, for letters of approval of the Uhlenhuth method of blood examination from the Ministers of Justice in Prussia, Austria, Wurtemburg, and Baden are published in the middle of this original work. Such letters of recommendation appearing in the book seem hardly the thing to our idea, but perhaps the opinion of judges on medico-legal work is of value to readers of science, and the official recognition of State work by State officials is *comme il faut*. The technique and method of biological experiments to differentiate between different kinds of flesh are discussed in 38 pages.

Fresh, frozen, dried, smoked, pickled, cooked, and putrid meat all come under notice. Horse flesh in sausages is soon detected by the fixation of the complement method.

The book concludes with 43 pages on the mode, detail of obtaining, and preservation of sera. There is a useful little chapter with three

illustrations on the procedure of inoculating material into the experimental rabbit.

Nuttall's quantitative method of estimating precipitates is given and illustrated, as also those of Wassermann and Schütze, Uhlenhuth and Beúmer.

The book would seem to be the most comprehensive and complete that has yet been written on biological albumen reactions. The practical application of the science to meat inspection and criminal investigations indicates its importance.

Bashford, Nuttall, Hewlett, and Rowland are the names of our countrymen whose contributions on the subject are called upon by the authors.

Translations.

UNILOCULAR HYDATID ECHINOCOCCUS IN THE LIVER OF A HORSE.

BY JOEST.

THE Institute at Dresden received the liver of a horse, aged 15, that had been slaughtered. The organ was broken up with echinococci, but with the exception of an echinococcus as big as a hen's egg in the lungs, there were no further changes in the viscera.

The weight of the liver was 22·3 kilogrammes (about 49 lb.) and it was about five times as big as a normal one. The organ showed fifteen echinococci cysts from a hen's egg to a man's head in size. The intermediate liver tissue between the cysts seemed only to act as a bond of union between the bladders.

Eleven cysts contained clear fluid; the echinococcal membrane was white, and showed numerous scolices. Two cysts contained brownish-red fluid, and numerous daughter bladders, from a pea to a hazel nut in size, which bore scolices on their internal surface. This was a fertile unilocular hydatid echinococcus. The cysts had thick capsules and were large, showing that they had been in existence some time. The case is noteworthy on account of the size and age of the cysts, and because the known echinococci form seldom occurs in the horse.

Histologically, in the peripheral layers of the membranes of the cysts were fine elastic fibres, as well as blood-vessels and numerous bile-duct elements, often without any lumen. The cells of the adjacent liver tissue showed pressure atrophy, especially on the surface of the organ where the rising cysts had pressed. Eosinophile cells were found in considerable quantity in the deeper layers of the connective tissue capsule, and were most numerous in the young echinococci.

PEROSOMUS CLUMBIS IN CALVES.

THREE cases were sent to the Institute by Veterinary Surgeon Hartmann, and Dr. Kabitz.

The anatomical appearances were in all cases similar. Head, neck, and fore part of the body showed great development, and hind part, proportionately, much too small. Vertebræ of the loins, tail,

and sacrum absent. The pelvis was affixed to the thorax by the thoracic vertebræ, skin, connective tissue, and hypoplastic muscular tissue.

Twelve pairs of ribs were present. The thoracic vertebræ ended at the eleventh rib. Thoracic organs normal. No internal genital organs in one case; in another case the male organs and bladder were present, and in the third the abdominal organs were normal.

(*From Report of the Imperial Veterinary College at Dresden.*)

EXPERIMENTAL AND HISTOLOGICAL OBSERVATIONS ON THE MILK AND AMNIOTIC FLUID OF A RABID SHEEP.

BY DR. R. REPETTO, SASSARI.

A MAD dog got into a herd of sheep and fourteen of them died of rabies. On these sheep, which were pregnant, the author made the following examinations:—

(1) Experiment for Negri's bodies in the horns of the amnion of the sheep.

(2) Also in those of the fœtus.

(3) Examination for the virus of rabies in milk pressed out of the udder of sheep.

(4) Testing for the virus in the amniotic fluid.

In the horns of the amnion of sheep, Negri's bodies were found, but not in those of the fœtus. Rats inoculated with the latter material did not contract the disease. Further, by inoculation of milk and amniotic fluid the illness was not caused.

The author arrives at the following conclusions:—

(1) That the virus of rabies does not pass from the mother to the fœtus, as Pasteur, Celli, L. le Blasi, and Zagari had proved, whilst Perroncito and Carita Loir affirmed the opposite.

(2) That Negri's bodies do not go through the placental filter, and, consequently, do not reach the fœtus.

(3) That the amniotic fluid contains no virus.

(4) That the milk contains no virus, as Pasteur, Celli, L. de Blasi, and Zagari had proved.

(*Deutsche Tierärztliche Wochenschrift*).

PERFORATION OF THE VAGINA AT THE TIME OF SERVICE IN A HEIFER.

BY M. RAOUL PARENT, VETERINARY SURGEON, OF SAINT DENIS.

As this is an accident of some rarity, I am taking the opportunity of recording it. On May 19, 1903, I was called by M. P., a master mason of F., to visit a Normandy heifer, aged 18 months, bought on November 24, 1902, at the fair of Maisse (Seine et Oise).

The animal had always been in perfect health from the time she was bought up to May 16, when she ceased to take all solid nourishment, and only took a little gruel. This inappetence was the cause of my attendance.

Examination showed: Temperature, 40° C.; pulse, 55; respirations, 12; back arched, hair dull and staring; rumination absent for two days, movements of the rumen spanned out, one every three minutes; excrement rarely passed, well moulded; micturition painful, but urine is of normal character.

The owner tells me that the heifer was taken to the bull on March 24 without success, and was presented a second time on May 16 at 7 o'clock in the morning. She was then served by a bull, aged 4, with full force, and he had not "worked" at all for some days. The coupling was made rapidly, and the heifer, in spite of strong pressures on the lumbar region, had preserved the arched back since then.

With the hand in the rectum I explored the pelvic cavity, and I found to the left on the floor of the basin a tumefaction the size of a duck's egg, painless, and pressure on which brings a little pus of repulsive odour between the lips of the vulva.

The diagnosis was clear; I had a perforation of the vagina by the penis of the bull and a subsequent abscess to deal with. The narrowness of the vulva hinders all useful surgical intervention, and the owner sends the heifer to the butcher on May 27.

At the autopsy on the exposed vagina a little in the front of the urinary meatus there is a small opening, the extremity of a fistula 6 cm. long, communicating with a pocket with very resistant walls, enclosing about 100 grammes of thick, creamy pus of bad smell. The other organs showed nothing abnormal.

(*Revue Générale de Médecine Vétérinaire.*)

QUICK HEALING OF QUITTOR AFFECTING THE CARTILAGE AFTER OPEN RESECTION OF THE CARTILAGE AND EXTIRPATION OF A PIECE OF CORONARY SKIN, AND APPLICATION OF AN OCCLUSIVE BANDAGE.

BY PROFESSOR L. HOFFMANN, OF STUTTGART.

HOFFMANN now always removes a piece of skin *entirely* from the coronet in operating for quittor. He prepares the site of the operation, rasps the horn thin, exposes the cartilage, cuts most of it out, and removes the rest with a curette. The loss of skin at the coronet is not very great, generally about 6 to 7 cm. long and about 2 cm. vertically. The operation is conducted under narcosis, bloodlessly and aseptically. The wound is powdered with iodoform, covered at first with iodoform gauze, and afterwards with tampons, a very firm bandage applied, a boot used, and the horse put in slings, and the bandage changed for the first time after fourteen days. As a rule healing has so far advanced that no second bandage is necessary. After fourteen days' occlusive bandaging the whole of the surface of the wound is covered with epithelium and cicatrizing horn; only the edge of the skin has a white, round epithelial layer, and the bits of horn have not quite covered the whole space. The unhealed portion is only small. In summer, if the foot bandage is soaked with blood and begins to smell, he gives a foot-bath of deodorizing solution

of permanganate of potash. The bandage is kept on and only removed if general bad appearances develop and temperature rises above 40° C In such cases recovery is not so quick as where an uninterrupted fourteen days' occlusion bandaging has been applicable.—

(*Berliner Thierärztliche Wochenschrift.*)

Correspondence.

LACK OF UNIFORMITY IN MEAT INSPECTION.

[We have received the following circular letter, with the appended resolution, issued by the Association of Veterinary Officers of Health. The strong case made out requires no comment from us beyond saying that we are in complete agreement and that we go a step further; the whole matter should refer to England and Wales and Ireland, as well as to Scotland.—Ed. *V. J.*]

ASSOCIATION OF VETERINARY OFFICERS OF HEALTH

To the Editors of the Veterinary Journal.

Sirs,—I have been instructed by the members of the above Association to bring under your notice the unsatisfactory conditions under which meat inspection and adjudication are at present carried on in Scotland.

The Royal Commission on Tuberculosis, reporting in 1898, states that—"Chaos is the only word to express the absence of system in the inspection and seizure of tuberculous meat. . . . The evils arising from this want of uniformity are manifold. . . . Very strong representations were laid before us on the part of butchers and meat traders, and also on behalf of the agriculturists who supply the butchers, as to the effect of this want of uniformity upon their business. It is obvious, we think, that these complaints are well founded. Producers and traders are making no unreasonable demand when they ask that a recognized standard should be observed, and that meat which, after inspection, is pronounced fit for sale in one market should not be liable to seizure in another because the inspecting authority happens to differ in opinion as to the extent of tuberculosis which may be dangerous." (Page 8, Sections 22 and 23.)

To remedy this chaotic situation the Commission framed recommendations which they considered necessary for the guidance of meat inspectors when dealing with carcases affected with tuberculosis, and the Local Government Board for Scotland issued these recommendations; but these proved abortive, owing to lack of that precision and detail which can only be secured under the direction of a veterinarian conversant with the work, and consequently in 1904—six years later—we find the Select Committee on the Tuberculosis (Animals) Compensation Bill, after hearing evidence from all parties interested, reporting "that the difficulty which stands in the way of the general adoption of a system of mutual insurance is the variety of practice which at present exists with regard to the amount of tubercular deposit, the existence of which in a carcase is held to justify its total

condemnation," and "that power should be given to the appropriate central authority in England, Scotland, and Ireland respectively, to enforce uniformity in this matter upon all local authorities" (Special Report, page 3, Section 2, second par.); and even so recently as in 1908 Dr. Dittmar, Medical Inspector to the Local Government Board for Scotland, urges: "It would be desirable, both in the public and in the traders' interest, if there were a greater degree of uniformity in the practice of different abattoirs in this connection" (Report on "Public Slaughter-houses (Scotland) and Meat Inspection," page 64).

The futility of the efforts made by the central authority as at present constituted being thus clearly shown in the highest official documents, it must accordingly be evident that the time is more than ripe for a strong representation from this Association, constituted as it is of veterinary surgeons approved under Section 43 of the Public Health (Scotland) Act, 1897, and actively engaged in the work of meat inspection and adjudication in different districts throughout Scotland.

At their meeting in the Municipal Buildings, Glasgow, on 5th current, attended by a large number of members from all parts of Scotland, and after full discussion of the whole matter, the resolution, of which a copy is appended, was unanimously adopted. Briefly put, its terms are (1) to standardize all conditions which render meat unsuitable for human food, and (2) to secure the appointment of a veterinary surgeon on the staff of the Local Government Board for Scotland. In addition, a petition of similar purport has been signed by all the Scottish members of this Association, numbering thirty-five, for presentation to the Secretary for Scotland and President of the Local Government Board for Scotland. The adoption of the measures therein advocated has proved effective in all other countries possessing the slightest claim to importance where the veterinary profession is entrusted not only with the practical work of meat inspection throughout the provinces or districts, but also with the task of *formulating* and *controlling* from the administrative centre the method and standard employed throughout the country. In this country, on the other hand, there is absolutely no *control* of the work, nor has there been any attempt even to *formulate* what is and what is not fit for human food, except in the abortive case cited. The veterinary profession has not been accorded its proper status in this connection, notwithstanding that it cannot be denied that it has long ere this justified its claim to be classed as one of the scientific professions, and the only one of these which possesses the training and intimate knowledge of comparative pathology that is requisite for carrying out meat inspection in a scientific manner. This country's freedom from certain animal plagues —such as cattle plague and foot-and-mouth disease—is alone one solid testimony to the scientific knowledge, energy, and loyalty of its members.

The members of this Association consider that the accompanying resolution is equally regardful of all the best interests of the country —the public, the trader, the stockowner, and the inspector alike, and on behalf of the Association I respectfully request that you use your influence with the Secretary for Scotland and the Local Government Board for Scotland to the end that throughout Scotland all meat for human food be submitted to a method of inspection and standard of

adjudication to be prescribed by the Board, and that a veterinary surgeon, with practical experience in the work, be appointed to the staff of the Local Government Board for Scotland, in order to ensure the uniform observance of the system.

I am, Sirs,

Your obedient servant,

A. M. TROTTER, M.R.C.V.S.,
Secretary.

Moore Street Abattoir,
Glasgow,
November 13, 1909.

RESOLUTION.

"Whereas we are of opinion that the great diversity existing in the systems of supervision observed by the local authorities throughout Scotland with regard to the meat supply is due to lack of control by the central authority, resolved that we petition the Secretary for Scotland and President of the Local Government Board for Scotland to prescribe a method of inspection and standard of adjudication applicable to all injurious or dangerous conditions occurring in carcases of animals used for human food, and to appoint to the staff of the Board a veterinary surgeon, with practical experience of the work, for the purpose of establishing and maintaining the uniform observance of such method and standard in the districts of all the local authorities throughout Scotland."

Books and Periodicals, &c., Received.

Proceedings of the Royal Society of Medicine; Bulletin of United States America Department of Agriculture; Bulletin of the Sleeping Sickness Bureau; Rhodesian Agricultural Journal; Transvaal Agricultural Journal; Massachusetts State Board of Agriculture; Memoirs of the Indian Civil Veterinary Departments; Report of the Ceylon Agricultural Society; Report of the Civil Veterinary Department in India; Report of the Bengal Veterinary College; Report of the Punjaub Veterinary College; Report of the Veterinary-Surgeon to the City of Glasgow; Tropical Agriculturist; Agricultural Journal of the Cape of Good Hope; London University Gazette.

Letters and Communications, &c.

Mr. H. W. Percy; Professor Nuttall; Mr. D. Farwell; Mr. E. A. Wilshaw; Mr. Payne; Professor Mettam; Mr. S. J. Motton; Spratt's Patent Limited; Mr. L. E. W. Bevan.

NOTE.—All communications should be addressed to 8, Henrietta Street, Covent Garden, London, W.C. Telephone, 4646 Gerrard. Telegrams, "Baillière, London."

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